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(54) Title: IMAGING PROTOCOLS

(57) Abstract: Protocols for radioimaging an event or disorder are provided. An exemplary protocol comprises a method of radioimaging a myocardial perfusion, the method comprising in sequence: (a) administering to a subject about 3 mCi Tl201 thallous chloride; (b) allowing said subject to rest; (c) radioimaging a heart of said subject; (d) subjecting said subject to a physical stress; (e) administering to said subject at a peak of physical stress about 20-30 mCi Tc99m sestamibi; and (f) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

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IMAGING PROTOCOLS

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to protocols for nuclear imaging, and more particularly, to protocols for nuclear imaging, without coincidence, with sensitivity which meets, and even outperforms that of PET, in terms of speed and spatial resolution, and with a high spectral resolution not available in PET.

Radionuclide imaging aims at obtaining an image of a radioactively labeled substance, that is, a radiopharmaceutical, within the body, following administration, generally, by injection. The substance is chosen so as to be picked up by active pathologies to a different extent from the amount picked up by the surrounding, healthy tissue; in consequence, the pathologies are operative as radioactive-emission sources and may be detected by radioactive-emission imaging. A pathology may appear as a concentrated source of high radiation, that is, a hot region, as may be associated with a tumor, or as a region of low-level radiation, which is nonetheless above the background level, as may be associated with carcinoma.

A reversed situation is similarly possible. Dead tissue has practically no pick-up of radiopharmaceuticals, and is thus operative as a cold region.

The mechanism of localization of a radiopharmaceutical in a particular organ of interest depends on various processes in that particular organ such as antigen-antibody reactions, physical trapping of particles, receptor site binding, removal of intentionally damaged cells from circulation, and transport of a chemical species across a cell membrane and into the cell by a normally operative metabolic process. A summary of the mechanisms of localization by radiopharmaceuticals is found in http://www.lunis.luc.edu/nucmed/tutorial/radpharm/i.htm.

The particular choice of a radionuclide for labeling antibodies depends upon the chemistry of the labeling procedure and the isotope nuclear properties, such as the number of gamma rays emitted, their respective energies, the emission of other particles such as beta or positrons, the isotope half-life, and the decay scheme.

In PET imaging, positron emitting radio-isotopes are used for labeling, and the imaging camera detects coincidence photons, the gamma pair of 0.511 Mev, traveling in opposite directions. Each coincident detection defines a line of sight, along which annihilation takes place. As such, PET imaging collects emission events, which

occurred in an imaginary tubular section enclosed by the PET detectors. A gold standard for PET imaging is PET NH_3 rest myocardial perfusion imaging with N-13-ammonia (NH_3), at a dose level of 740 MBq, with attenuation correction. Yet, since the annihilation gamma is of 0.511 Mev, regardless of the radio-isotope, PET imaging does not provide spectral information, and does not differentiate between radio-isotopes.

In SPECT imaging, primarily gamma emitting radio-isotopes are used for labeling, and the imaging camera is designed to detect the actual gamma emission, generally, in an energy range of approximately 11-511 KeV. Generally, each detecting unit, which represents a single image pixel, has a collimator that defines the solid angle from which radioactive emission events may be detected.

Because PET imaging collects emission events, in the imaginary tubular section enclosed by the PET detectors, while SPECT imaging is limited to the solid collection angles defined by the collimators, generally, PET imaging has a higher sensitivity and spatial resolution than does SPECT. Therefore, the gold standard for spatial and time resolutions in nuclear imaging is defined for PET.

Although radiopharmaceuticals are powerful labeling tools, their recommended maximum dose must be taken into account when using these agents for imaging. In order to minimize exposure to the tissue, radiopharmaceuticals, which have a long half life, and radiopharmaceuticals, which have radioactive daughters, are generally avoided.

The recommended maximum doses of radiopharmaceuticals are 5 rems for a whole body dose and 15 rads per organ, while the allowable dose for children is one tenth of the adult level. The per-organ criterion protects organs where accumulation takes place. For example, radiopharmaceuticals for which removal is primarily by the liver should be administered at a lower dose than those for which removal is partly by the liver and partly by the kidney, because in the former, a single organ is involved with the removal, and in the latter, there is sharing of the removal.

Radiopharmaceutical behavior in vivo is a dynamic process. Some tissues absorb radiopharmaceuticals faster than others or preferentially to others, and some tissues flush out the radiopharmaceuticals faster than others or preferentially to others, so the relative darkness of a given tissue is related to a time factor. Since the uptake clearance of such a radiopharmaceutical by the various tissues (target and

background) varies over time, standard diagnosis protocols usually recommend taking an image at the time at which the ratio of target emission versus background emission is the highest.

Yet, this approach produces a single parameter per voxel of the reconstructed image, a level of gray, at a specific time, and ignores the information that could be obtained from the behavior of a radiopharmaceutical as a function of time.

Dynamic imaging, on the other hand, attempts to acquire the behavior of a radiopharmaceutical as a function of time, for example, to measure perfusion in myocardial tissue. Dynamic imaging is advantageous to static imaging, as it provides a better measure of blood flow, it is more sensitive to ischemia than static imaging, and both perfusion as absolute blood flow and coronary flow reserve as well as myocardial viability may be obtained from a single imaging session.

It is possible to design highly sensitive SPECT imaging cameras with the sensitivity and resolution of PET imaging cameras. For example, PCT IL2006/000059 assigned to Spectrum Dynamics LLC., discloses a highly sensitive radioactive-emission camera, which opens a new realm in SPECT-type imaging. Unlike other SPECT imaging cameras, this camera is viable for dynamic studies. Accordingly, it may be used to compare the rates of change of radiopharmaceutical in a tissue with spectral resolution. Other SPECT imaging cameras are only capable of measuring the total concentration of a radiopharmaceutical in a tissue. As mentioned above, this is particularly important for measuring cardiac functions such as cardiac ejection parameters.

The camera disclosed in PCT IL2006/000059 is capable of faster and lower dose imaging compared to other SPECT cameras. The higher sensitivity of this camera also allows for use of new agents which in existing systems would not produce sufficient radioactivity.

The camera is also able to make use of radiopharmaceutical cocktails and dynamic imaging of multiple isotopes. Thus, dual and multiple isotope studies may be performed using spectral resolution. This may be particularly relevant for tumor diagnosis, since in some cases the difference between tumor and healthy tissue is that one picks up two agents whilst the other picks up only one of the agents as well as different radiopharmaceutical kinetics between tumor and healthy tissue.

There is an urgent need for and it would be particularly advantageous to have novel protocols with clear guidelines that may be used for nuclear imaging with SPECT cameras of high sensitivity and resolution.

SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 10-15 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected about 2 minutes following step (c);

(4) step (f) is effected about 30-60 minutes following step (d); and

(5) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is affected as described in Table 1.

According to another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (f) is effected about 30-60 minutes following step (e); and

(5) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is affected as described in Table 2.

According to yet another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 2 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is effected immediately following step (e);

(6) step (f) is for about 2 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 3.

According to still another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is immediately following step (a);

(2) step (b) is for about 2 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 2 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 4.

According to an additional aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject immediately following the peak stress, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15 minutes;

(2) step (c) is for about 2 minutes;

(3) step (e) is effected about 30 - 60 minutes following step (d); and

(4) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 5.

According to yet an additional aspect of the present invention there is provided method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 20-30 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 3 mCi Tl201 thallous chloride;

(f) radioimaging the heart of the subject; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15-30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (f) is effected about 10-15 minutes following step (e);

(5) step (f) is for about 4 minutes;

(6) step (g) is effected about 4 hours following step (f); and

(7) step (g) is for about 6 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 6.

According to still an additional aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(f) radioimaging the heart of the subject; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15-30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is effected immediately following step (e);

(6) step (f) is for about 4 minutes;

(7) step (g) is effected about 4 hours following step (f);

(8) step (g) is for about 6 minutes; and

(9) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 7.

According to a further aspect of the present invention there is provided method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(e) radioimaging the heart of the subject; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a);

(2) step (b) is for about 2 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 4 minutes;

(7) step (f) is effected about 4 hours following step (e);

(8) step (f) is for about 6 minutes;

(9) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 8.

According to yet a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(f) allowing the subject to rest; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is for about 2 minutes;

(6) step (g) is effected immediately following step (f);

(7) step (g) is for about four minutes; and

(8) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 9.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m Teboroxime;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m Teboroxime; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following or during step (a);

(2) step (b) is for about 2-10 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following or during step (d);

(6) step (e) is for about 2-10 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 10.

According to still a further aspect of the present invention there is provided a method of radioimaging a lung perfusion, the method comprising simultaneously:

(a) administering to a subject less than about 5 mCi Tc99m Diethylene triamine-pentacetic acid (DTPA);

(b) administering to a subject less than about 5 mCi Tc99m MAA;

(c) radioimaging a lung of the subject, thereby radioimaging a lung perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) the Tc99m Diethylene triamine-pentacetic acid (DTPA) is administered via a nebulizer;

(2) step (c) is for about 0-30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 11.

According to still a further aspect of the present invention there is provided a method of radioimaging a bone inflammation or a bone cancer, the method comprising simultaneously:

(a) administering to a subject about 20-30 mCi Tc99m MDP; and

(b) radioimaging a bone of the subject, thereby radioimaging a bone inflammation or a bone cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 0-60 minutes following step (a);

(2) step (b) is for about six minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 12.

According to still a further aspect of the present invention there is provided a method of radioimaging an inflammatory process, the method comprising in sequence:

(a) administering to a subject about 2-3 mCi In 111 WBC; and

(b) radioimaging the subject, thereby radioimaging an inflammatory process.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a).

(2) step (b) is for about 1 minute.

According to still further features in the described preferred embodiments the method is effected as described in Table 13.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical stress;

(d) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10-15 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is immediately following step (b);

(4) step (e) is effected about 30-60 minutes following step (d); and

(5) step (e) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 14.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical stress;

(d) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 15-30 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (e) is effected about 30-60 minutes following step (d); and

(5) step (e) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 15.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) subjecting the subject to a physical stress;

(c) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(d) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a);

(2) step (d) is effected about 30-60 minutes following step (c); and

(3) step (d) is for about 5-15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 16.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 15 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 17.

According to still a further aspect of the present invention there is provided a method of radioimaging a breast cancer, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tc99m sestamibi; and

(b) radioimaging a breast of the subject, thereby radioimaging a breast cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 15-30 minutes following step (a);

(2) step (b) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is, effected as described in Table 18.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) simultaneously administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO), no more than about 3 mCi Tc99m ECD and no more than about 5 mCi I123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 19.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 20.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 3 mCi Tc99m ECD; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 21.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 22.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 23.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi Tc99m ECD; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 24.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 25.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver structure, the method comprising simultaneously:

(a) administering to a subject about 0.5 mCi Tc99m mebrofenin; and

(b) radioimaging a liver of the subject, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 26.

According to still a further aspect of the present invention there is provided a method of radioimaging a lung perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi of Tc99m DTPA and no more than 0.5 mCi of MAA or DTPA ln 111; and

(b) radioimaging a lung of the subject, thereby radioimaging a lung perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for about 6 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 27.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (thallium rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 4 mCi of Tl thallous chloride, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, wherein step (a) is for about 2-20 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 28.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (thallium stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 4 mCi Tl201 thallous chloride; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 2-20 minutes; and

(3) the pharmacological stress adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 29.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (teboroxime rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m teboroxime, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 30.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (teboroxime stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 4 mCi Tc99m Teboroxime; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 2-20 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 31.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (sestamibi rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m sestamibi, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 32.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (sestamibi stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 20-30 mCi of Tc99m sestamibi; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 33.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (tetrofosmin rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m tetrofosmin, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 34.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (tetrofosmin stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 20-30 mCi of Tc99m tetrofosmin; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following or during step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 35.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (Q12 rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m Q12, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 36.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (Q12 stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 30 mCi of Tc99m Q12; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 37.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (BMIPP-I-123 rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 5 mCi of BMIPP I-123, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 38.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (BMIPP I-123 stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 5 mCi of BMIPP I-123; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 39.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 30 mCi of a radiopharmaceutical; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 10 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 40.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising simultaneously:

(a) radioimaging a heart of a subject; and

(b) administering to the subject about 30 mCi of a PET radiopharmaceutical, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 41.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, the method comprising simultaneously:

(a) radioimaging a tumor of a subject; and

(b) administering to the subject about 30 mCi of Tc99m Teboroxime, 30 mCi of Tc99m sestamibi, 30 mCi of Tc99m tetrofosmin or 4 mCi of Tl-201, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 5 minutes.

According to still further features in preferred embodiments of the invention described below, the method is effected as described in Table 42.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, the method comprising simultaneously:

(a) radioimaging a tumor of a subject; and

(b) administering to the subject about 4 mCi of Tl201 thallous chloride and no more than about 30 mCi of Tc99m sestamibi, thereby radioimaging a tumor.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 43.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising simultaneously:

(a) radioimaging a kidney of a subject; and

(b) administering to the subject about 1 mCi of Tc99mDTPA and about 3-10 mCi of Tc99mMAG3, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, step (a) is 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 44.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising simultaneously:

(a) radioimaging a kidney of a subject; and

(b) administering to the subject about 1 mCi of Tc99m DTPA and about 1 mCi of HippuranI-123, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, step (a) is about 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 45.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) radioimaging a brain of a subject; and

(b) administering to the subject about 20 mCi of Tc99m ECD (neurolite) and about 20 mCi of HPMAO 99m labeled and about 5 mCi of SpectamineI123, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 46.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) radioimaging a brain of a subject; and

(b) administering to the subject no more than about 20 mCi of teboroxime, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 47.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver structure, the method comprising simultaneously:

(a) radioimaging a liver of the subject; and

(b) administering to the subject no more than about 5 mCi of Tc99m sulfur colloid, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (a) is no more than 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 48.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver function, the method comprising simultaneously:

(a) radioimaging a liver of the subject; and

(b) administering to the subject no more than about 10 mCi of Tc99m disida, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (a) is effected every five minutes for up until 1 hour.

According to still further features in the described preferred embodiments the method further comprises administering an agent for gall bladder contraction 1 hour following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 49.

According to still a further aspect of the present invention there is provided a method of radioimaging a gastric emptying, the method comprising simultaneously:

(a) radioimaging a stomach of a subject; and

(b) administering to the subject about 3 MBq of Tc99m Sulfer colloid or labeled solid food or 0.5 MBq In-111 DTPA labeled liquid food, thereby radioimaging a gastric emptying.

According to further features in preferred embodiments of the invention described below, step (a) is for a time until the stomach is empty of the labeled food.

According to still further features in the described preferred embodiments the method is effected as described in Table 50.

According to still a further aspect of the present invention there is provided a method of radioimaging a cardiac vulnerable plaque, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Tc99m annexin and no more than about 5mCi Tc99m AccuTec; and

(b) radioimaging a blood vessel of the subject, thereby radioimaging a cardiac vulnerable plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 51.

According to still a further aspect of the present invention there is provided a method of radioimaging for prostate cancer, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Prostascint containing 111In capromab pendetide; and

(b) radioimaging a prostate of the subject, thereby radioimaging for prostate cancer.

According to further features in preferred embodiments of the invention described below, the method comprises comprising at least one or more of the following:

(1) step (b) is effected about 24 - 72 hours following step (a);

(2) step (b) is less than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 52.

According to still a further aspect of the present invention there is provided a method of radioimaging for SST receptor expressing tumors, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Octreotide containing 111 In DTPA; and

(b) radioimaging a body of the subject, thereby radioimaging for SST receptor expressing tumors.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 53.

According to still a further aspect of the present invention there is provided a method of radioimaging for neuroendocrine tumors, the method comprising in sequence:

(a) administering to a subject no more than about 20 mCi Tc99m Neotec; and

(b) radioimaging a body of the subject, thereby radioimaging for neuroendocrine tumors.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is less than about 30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 54.

According to still a further aspect of the present invention there is provided a method of radioimaging for thrombii, the method comprising in sequence:

(a) administering to a subject no more than about 20 mCi Tc99m Acutec; and

(b) radioimaging blood vessels of the subject.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected from about 0-20 minutes following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 55.

According to still a further aspect of the present invention there is provided a method of radioimaging a pheochromocytoma and/or myocardial failure, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi I-123 iofetamine hydrochloride MIBG; and

(b) radioimaging an adrenal gland and/or heart of the subject, thereby radioimaging a pheochromocytoma and/or myocardial failure.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (b) is less than about 30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 56.

According to still a further aspect of the present invention there is provided a method of radioimaging a cardiac stress, the method comprising in sequence:

(a) administering to a subject about 4 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical or pharmacological stress, wherein the pharmacological stress is at least one vasodilatory agent; and

(d) radioimaging a heart of the subject, thereby radioimaging a cardiac stress.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 2 minutes following step (a);

(2) step (b) is for about 2-5 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected no more than about 5 minutes following step (c);

(5) step (d) is for about 2-10 minutes; and

(6) the at least one vasodilatory agent is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 57.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising in sequence:

(a) administering to a subject about 2-4 mCi DTPA and/or Tc99mMAG3;

(b) radioimaging a kidney of the subject;

(c) subjecting the subject to a physical and/or at least one pharmacological stress; and

(d) radioimaging a kidney of the subject.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 10-30 minutes;

(2) step (c) is effected immediately following step (b);

(3) step (d) is for about 10-30 minutes

(4) the pharmacological stress is selected from the group consisting of captopril fuside, a vasodilatory agent and a diuretic agent.

According to still further features in the described preferred embodiments the method is effected as described in Table 58.

According to still a further aspect of the present invention there is provided a method of radioimaging to determine Bexaar dosimetry, the method comprising simultaneously:

(a) radioimaging a body of a subject; and

(b) administering to the subject about 5 MCi/35 mg of I123 iofetamine hydrochloride, thereby radioimaging to determine Bexaar dosimetry.

According to further features in preferred embodiments of the invention described below, step (a) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 59.

According to still a further aspect of the present invention there is provided a method of radioimaging a parathyroid adenoma, the method comprising in sequence:

(a) administering to a subject about 1 mCi thallium 201thallous chloride and about 15mCi Tc99m pertechnetate;

(b) radioimaging a parathyroid of the subject, thereby radioimaging a parathyroid adenoma.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10 minutes following step (a); and

(2) step (b) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 60.

According to still a further aspect of the present invention there is provided a method of radioimaging a parathyroid adenoma, the method comprising in sequence:

(a) administering to a subject about 15 mCi Tc99m sestamibi and about 100 μCi I123;

(b) radioimaging a parathyroid of the subject, thereby radioimaging a parathyroid adenoma.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10 minutes following step (a); and

(2) step (b) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 61.

According to still a further aspect of the present invention there is provided a method of radioimaging a thyroid cancer, the method comprising in sequence:

(a) administering to a subject about 10 mCi Tc99m MDP and about 4 mCi I-131;

(b) radioimaging a thyroid of the subject, thereby radioimaging a thyroid cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 62.

According to still a further aspect of the present invention there is provided a method of radioimaging an endocrine tumor, the method comprising in sequence:

(a) administering to a subject about 15 mCi Tc99m MDP and about 4 mCi ln111 octeotride;

(b) radioimaging a body of the subject, thereby radioimaging an endocrine tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 63.

According to still a further aspect of the present invention there is provided a method of radioimaging an endocrine tumor, the method comprising in sequence:

(a) administering to a subject about 4 mCi ln111 octeotride;

(b) administering to a subject about 15 mCi Tc99m MDP;

(c) radioimaging a body of the subject, thereby radioimaging an endocrine tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 3 days following step (a);

(2) step (c) is effected no more than about 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 64.

According to still a further aspect of the present invention there is provided a method of radioimaging a prostate tumor, the method comprising in sequence:

(a) administering to a subject about 3 mCi ln111 capromab pentitide;

(b) administering to a subject about 15 mCi Tc99m RBCs;

(c) radioimaging a pelvis/abdomen of the subject, thereby radioimaging a prostate tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 3 days following step (a);

(2) step (c) is effected no more than about 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 65.

According to still a further aspect of the present invention there is provided a method of radioimaging a bone infection, the method comprising in sequence:

(a) administering to a subject about 3 mCi In111 WBC;

(b) administering to a subject about 15 mCi Tc99m colloid;

(c) radioimaging a bone of the subject, thereby radioimaging a bone infection.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than 3 days following step (a);

(2) step (c) is effected no more than 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 66.

According to still a further aspect of the present invention there is provided a method of radioimaging a neck or head cancer invasion of a bone or cartilage, the method comprising in sequence:

(a) administering to a subject about 2 mCi Tl201 thallous chloride and about 15 mCi Tc99m MDP;

(b) radioimaging a bone or cartilage of the subject, thereby radioimaging a neck or head cancer invasion of a bone or cartilage.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 67.

According to still a further aspect of the present invention there is provided a method of radioimaging a pathological condition, the method comprising in sequence:

(a) administering to a subject about 2 mCi In111WBCs;

(b) administering to the subject about 1 mCi Tl201 thallous chloride and about 10'mCi Tc99m sestamibi; and

(c) radioimaging a body of the subject, thereby radioimaging a pathological condition.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 days following step (a); and

(2) step (c) is for about 30 minutes.

(3) the pathological condition is selected from the group consisting of an infection, a tumor and a myocardial infection.

According to still further features in the described preferred embodiments the method is effected as described in Table 68.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial ischemia, the method comprising in sequence:

(a) administering to a subject about 2 mCi I123 BMIPP;

(b) administering to the subject about 1 mCi Tl201 thallous chloride and about 10 mCi of a Tc99m labeled chemical selected from the group consisting of sestamibi and teboroxime; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial ischemia.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 48 hours following step (a); and

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 69.

According to still a further aspect of the present invention there is provided a method of radioimaging a pathological condition or a fever of unknown origin, the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111WBC;

(b) administering to the subject about 15 mCi 99m Fanoselomab; and

(c) radioimaging a body of the subject, thereby radioimaging a pathological condition or a fever of unknown origin.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a); and

(2) step (c) is for about 30 minutes.

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 70.

According to still a further aspect of the present invention there is provided a method of radioimaging to indicate schizophrenia or Parkinson's disease, the method comprising in sequence:

(a) administering to a subject about 2 mCi I123 IBZM;

(b) administering to the subject about 15 mCi Tc99m HMPAO; and

(c) radioimaging a brain of the subject, thereby radioimaging to indicate schizophrenia or Parkinson's disease.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a); and

(2) step (c) is for about 30 minutes.

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 71.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, a tumor perfusion and/or for differentiating a tumor from infection the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111 WBC;

(b) administering to the subject Tc99m sestamibi, Tc99m ArcitumoMab and Tl201 thallous chloride; and

(c) radioimaging an organ and/or a body of the subject, thereby radioimaging for identifying a tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected about 5 minutes following step (b);

(4) a dose of Tc99m sestamibi and Tc99m Arcitumo Mab is each about 10 mCi; and

(5) a dose of Tl201 thallous chloride is about 1 mCi.

According to still further features in the described preferred embodiments the method is effected as described in Table 72.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising in sequence:

(a) administering to a subject about 2 mCi Iln111 DTPA;

(b) administering to the subject about 15 mCi Tc99m MAG3; and

(c) radioimaging a kidney of the subject, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected about 5 minutes following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 73.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor perfusion, the method comprising in sequence:

(a) administering to a subject about 1 mCi Tl thallous chloride;

(b) administering to the subject about 15 mCi Tc99m teboroxime or about 15 mCi Tc99m sestamibi; and

(c) radioimaging an organ of the subject, thereby radioimaging a tumor perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 74.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion and apoptosis in blood vessel plaque, the method comprising in sequence:

(a) administering to a subject about 1 mCi Tl thallous chloride;

(b) administering to the subject about 15 mCi Tc99m Annexin; and

(c) radioimaging a heart and blood vessels of the subject, thereby radioimaging a myocardial perfusion and apoptosis in blood vessel plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected less than about 1 hour following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 75.

According to still a further aspect of the present invention there is provided a method of radioimaging to differentiate between infection and bone marrow activation, the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111WBC;

(b) administering to the subject about 15 mCi Tc99m sulfur colloid; and

(c) radioimaging a body of the subject, thereby radioimaging a tumor perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 76.

According to still a further aspect of the present invention there is provided a method of radioimaging an osteomyelitis, the method comprising in sequence:

(a) administering to a subject about 2 mCi In111WBC;

(b) administering to the subject about 15 mCi Tc99m MDP; and

(c) radioimaging a bone of the subject, thereby radioimaging an osteomyelitis.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 77.

According to still a further aspect of the present invention there is provided a method of radioimaging an inflammation, the method comprising in sequence:

(a) administering to a subject about 5 mCi Gallium 67;

(b) administering to the subject about 15 mCi In111WBCs; and

(c) radioimaging a body of the subject, thereby radioimaging an inflammation.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes; and

(3) step (c) is effected about 72 hours following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 78.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion and apoptosis in blood vessel plaque, the method comprising in sequence:

(a) administering to a subject about 2 mCi In111 annexin;

(b) administering to the subject about 15 mCi Tc99m teboroxime or about 2 mCi Tl201 thallous chloride; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion and apoptosis in blood vessel plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected no more than about 3 minutes following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 79.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 2 mCi Tl201 thallous chloride;

(b) administering to the subject about 15 mCi Tc99m pyrophosphate; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial infusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes; and

(3) step (c) is effected about 1 hour following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 80.

A method of radioimaging a myocardial perfusion, the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 15 mCi of Tc99m pyrophsophate and about 2 mCi of Tl 201 thallous chloride, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 81.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion or cardiac vulnerable plaque, the method comprising simultaneously:

(a) administering to a subject about 5 mCi In111 annexin;

(b) administering to the subject about 5 mCi Tc99m Accutec;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject about 1 mCi Tl201 thallous chloride; and

(e) radioimaging a heart and blood vessels of the subject, thereby radioimaging a myocardial perfusion or cardiac vulnerable plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is effected immediately following step (b);

(3) the pharmacological stress is adenosine or dipyridamole;

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 82.

According to still a further aspect of the present invention there is provided a method of radioimaging a glucose metabolism, the method comprising simultaneously:

(a) administering to a subject about 30-50 mCi FDG; and

(b) radioimaging a body of the subject, thereby radioimaging a glucose metabolism.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a); and

(2) step (b) is for less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 83.

According to further features in preferred embodiments of the invention described below the imaging is effected using a camera which comprises:

(i) at least one radioactive-emission detector designed and constructed to image radioactive emission from the tissue or body;

(ii) a position-tracking device communicating with the at least one radioactive-emission detector and configured to provide positional information for the at least one radioactive-emission; and

(iii) a data processor, designed and configured for receiving data inputs from the position tracking device and the at least one radioactive-emission detector, and for generating an image of the tissue or body.

According to still another aspect of the present invention there is provided a method of packaging a radiopharmaceutical selected from the group consisting of Tl201 thallous chloride, Tc99m sestamibi, Tc 99m Teboroxime, Tc 99m DTPA, MAA, Tc 99m MDP, In 111 WBC, Tc 99m exametazine (HMPAO), Tc 99m ECD, I 123 isofetamine hydrochloride, I 123 isofetamine hydrochloride, Tc 99m mebrofenin, DTPA In 111, tetrofosmin, Tc 99m MAG3, Hippuran I-123, neurolite, Tc 99m sulfur colloid, Tc 99m disida, Tc99m Annexin, Tc99m AccuTec, Prostascint containing 111 In DTPA, Octreotide containing 111 In DTPA, Tc 99m neotec, MIBG containing I 123 iofetamine hydrochloride, Tc 99m pertechnetate, I 123, Tc 99m MDP, In 111 capromab pentitide, Tc 99m RBC, I 123 BMIPP, Tc 99m Fanoselomab, I 123 IBZM, Tc 99m ArcitumoMab, Gallium 67, Tc 99m pyrophosphate, In 111 annexin, F-18-Fluorodeoxyglucose (FDG), F-18-Fluoromisonidazole, F-18-3'-Fluoro-3'-deoxythymidine (FLT), F-18-Fluoromethyl choline (FCH), F-18-4-Fluoro-m-tyrosine (FMT), F-18-6-Fluoro-L-DOPA, F-18-FP-β-CIT, F-18-Pencyclovir (FHBG), F-18-Fuoroestradiol (FES), C-11-Methionine, Tc-99m-P280, Acutect®, C-11-Raclopride, I-123-iodobenzamide (IBZM), C-11-carfentanil, C-11-α-methyl-L-tryptophan, C-115-Hydroxytryptophan, F-18-MPPF, F-18-Altanserin, C-11-Acetate, C-11-Palmitate and F-18-Fluorodopamine, the method comprising packaging the radiopharmaceutical in a package and providing in association with the package in printed and/or electronic form instruction of use according to any of the methods of the preceding claims.

According to yet another aspect of the present invention there is provided an article of manufacturing produced according to the above packaging method.

According to yet another aspect of the present invention there is provided a diagnostic pharmaceutical kit comprising a packaged dose unit of a diagnostic radiopharmaceutical having a dose equivalent of 2.5 mrem or less per kg body weight.

According to yet another aspect of the present invention there is provided a packaged dose unit has a dose equivalent of 2 mrem or less per kg body weight.

According to further features in preferred embodiments of the invention described below packaged dose unit has a dose equivalent of 1 mrem or less per kg body weight.

According to yet another aspect of the present invention there is provided a packaged dose unit of diagnostic radiopharmaceutical having a dose equivalent of 150 mrem or less.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is a radiotracer.

According to further features in preferred embodiments of the invention described below a radioisotope and a recognition binding moiety of the radiotracer are packaged in individual containers.

According to further features in preferred embodiments of the invention described below a purity of a radioisotope of the diagnostic radiopharmaceutical is at least 60 %.

According to further features in preferred embodiments of the invention described below a purity of a radioisotope of the diagnostic radiopharmaceutical is at least 90 %.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{13}N-Ammonia and whereas the packaged dose unit comprises 0.01-5 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{18}F-Fludeoxyglucose and whereas the packaged dose unit comprises 0.1-3 mCi.

According to further features in preferred embodiments of the invention described below the the diagnostic radiopharmaceutical is ^{18}F-Sodium Fluoride and whereas the packaged dose unit comprises 0.1-3 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{81m}Kr-Krypton and whereas the packaged dose unit comprises 0.05-2 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{111}In-Indium Capromab pendetide and whereas the packaged dose unit comprises 0.01-2 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{99m}Tc-Technetium Arcitumomab and whereas the packaged dose unit comprises 0.05-5 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{111}In-Indium Pentetreotide and whereas the packaged dose unit comprises 0.005-1 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{125}I-Iodide Albumin and whereas the packaged dose unit comprises 0.0005-0.005 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{51}Cr-Sodium Chromate and whereas the packaged dose unit comprises 0.001-0.05 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{99m}Tc-Technetium Disofenin and whereas the packaged dose unit comprises 0.005-1 mCi.

According to further features in preferred embodiments of the invention described below the diagnostic radiopharmaceutical is ^{99m}Tc-Technetium Sestamibi and whereas the packaged dose unit comprises 0.01-5 mCi.

According to yet another aspect of the present invention there is provided a composition of matter comprising a low dose of at least one radiopharmaceutical intended for administration in whole to a human subject of a particular age and/or weight.

According to further features in preferred embodiments of the invention described below the low dose is a dose below the maximal dose allowable to be administered to the human subject of the particular age and/or weight.

According to further features in preferred embodiments of the invention described below the maximal dose is the lower of 5 REM and a dose that following administration and distribution in a body of the subject does note accumulate in any specific organ in the body in excess of 15 Rads.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is selected from the group consisting of [18F]Fluorodeoxyglucose (FDG), [18F]-Fluoromisonidazole, [18F]3'-Fluoro-3'-deoxythymidine (FLT), [18F]Fluoromethyl choline (FCH), [18F]4-Fluoro-m-tyrosie (FMT), [18F]6-Fluoro-L-DOPA, [18F]FP-βCIT, [18F]Pencyclovir (FHBG), [18F]Fuoroestradiol (FES), [11C]Methionine, 111In-Pentetreotide, 99mTc-P829, 99mTc-P280, 123I-VIP (vasoactive intestinal peptide), 131I-NP-59, [11C]Raclopride, 123I-IBZM, [11C]Carfentanil, [11C]α-methyl-L-tryptophan, [11C]5-Hydroxytryptophan, [18F]MPPF, [18F]Altanserin, [11C]Acetate, [11C]Palmitate, [18F]Fluorodopamine, ^{3}H-water, ^{3}H-inulin, ^{11}C-carbonmonoxide, ^{13}N-ammonia, ^{14}C-inulin, ^{15}O-H_2O, ^{15}O-O_2, ^{18}F-fluorodeoxyglucose, ^{18}F-sodium fluoride, ^{51}Cr-erythrocytes (RBC), ^{57}Co-vitamin B_{12} (cyanocobalamin), ^{58}Co-vitamin B_{12} (cyanocobalamin), ^{59}Fe-citrate, ^{60}Co-vitamin B_{12} (cyanocobalamin), ^{67}Ga-citrate, ^{68}Ga-citrate, ^{75}Se-selenomethionine, ^{81m}Kr-krypton for inhalation, oral administration or injections, ^{82}Rb, ^{85}Sr-nitrate, ^{90}Y/^{111}In-ibritumomab tiuxetan (^{90}Y/^{111}In-Zevalin), ^{99m}Tc-albumin microspheres, ^{99m}Tc-disofenin, lidofenin and mebrofenin, ^{99m}Tc-DMSA, ^{99m}Tc-DTPA (injection), ^{99m}Tc-DTPA (aerosol), ^{99m}Tc-ECD (ethylene cystate dimer), ^{99m}Tc-exametazime (HMPAO), ^{99m}Tc-glucoheptonate, ^{99m}Tc-HEDP, ^{99m}Tc-HMDP, ^{99m}Tc-HSA, ^{99m}Tc-MAA, ^{99m}Tc-MAG_3, ^{99m}Tc-MDP, ^{99m}Tc-tetrofosmin, ^{99m}Tc-sestamibi, ^{99m}Tc-oral administrations, ^{99m}Tc-pertechnetate, ^{99m}Tc-pyrophosphate, ^{99m}Tc-RBC *in vitro* and *in vivo* labeling, ^{99m}Tc-sulfur colloid, ^{99m}Tc-teboroxime, ^{99m}Tc-white blood cells, ^{111}In-ibritumomab tiuxetan (^{111}In-Zevalin), ^{111}In-DTPA, ^{111}In-platelets, ^{111}In-RBC, ^{111}In-white blood cells, ^{123}I-hippuran, ^{123}I-IMP, ^{123}I-mIBG, ^{123}I-sodium iodide, ^{124}I-sodium iodide, ^{125}I-fibrinogen, ^{125}I-IMP, ^{125}I-mIBG, ^{125}I-sodium iodide, ^{126}I-sodium iodide, ^{130}I- sodium iodide, ^{131}I-hippuran, ^{131}I-HSA, ^{131}I-MAA, ^{131}I-mIBG, ^{131}I-Rose Bengal, ^{131}I-sodium iodide, ^{127}Xe-inhalation and injection, ^{133}Xe-inhalation and injection, ^{197}Hg-chlormerodrin, ^{198}Au-colloid and ^{201}Tl-chloride, Cu-62, Ga-68, Indium-111 Capromab pendetide, Indium In-111 Satumomab Pendetide, Technetium Tc 99m Arcitumomab (CEA-Scan), Technetium

Tc 99m Fanolesomab, Technetium Tc 99m Nofetumomab Merpentan, Indium In 111 Oxyquinoline, Indium In 111 Pentetate, Indium In 111 Pentetreotide, Iobenguane, Radioiodinated, IofetamineI 123, Iothalamate Sodium I 125, Iodide 125 Albumin, Radioiodinated Albumin, SodiumChromate Cr 51, (Sodium) Pertechnetate Tc 99m, Technetium Tc 99m Depreotide, Technetium Tc 99m Apcitide, TechnetiumTc 99m Bicisate, Technetium Tc 99m Disofenin (HIDA), Chromic Phosphate, SR 89 Chloride (Metastron), Technetium Tc 99m Oxidronate, Technetium Tc 99m (Pyro- and trimeta-) Phosphates, Technetium Tc 99m Sulfur Colloid, Technetium Tc 99m HDP, Technetium Tc 99m Sulpher colloid and radiopharmaceuticals which comprise an idsotope selected from the group onsisting of ^{198}Au, ^{11}C, ^{14}C, ^{51}Cr, ^{57}Co, ^{58}Co, ^{60}Co, ^{62}Cu ^{18}F, ^{59}Fe, ^{67}Ga, ^{68}Ga, ^{3}H, ^{153}Sm, ^{197}Hg, ^{111}I, ^{123}I, ^{124}I, ^{125}I, ^{126}I, ^{130}I, ^{131}I, ^{133}I, ^{111}In, ^{81}Kr, ^{127}Xe, ^{133}Xe, ^{67}Cu, ^{177}Lu, ^{13}N, ^{15}O, ^{82}Rb, ^{117m}Sn, ^{85}Sr, ^{89}Sr ^{52}Fe, ^{113m}In, ^{99m}Tc, ^{201}Tl.

According to further features in preferred embodiments of the invention described below the low dose is selected from the group consisting of:

(i) less than 90 % of the maximal dose;
(ii) less than 85 % of the maximal dose;
(iii) less than 80 % of the maximal dose;
(iv) less than 75 % of the maximal dose;
(v) less than 70 % of the maximal dose;
(vi) less than 65 % of the maximal dose;
(vii) less than 60 % of the maximal dose;
(viii) less than 55 % of the maximal dose;
(ix) less than 50 % of the maximal dose;
(x) less than 45 % of the maximal dose;
(xi) less than 40 % of the maximal dose;
(xii) less than 35 % of the maximal dose;
(xiii) less than 30 % of the maximal dose;
(xiv) less than 25 % of the maximal dose;
(xv) less than 20 % of the maximal dose;
(xvi) less than 15 % of the maximal dose;
(xvii) less than 10 % of the maximal dose;
(xviii) less than 9 % of the maximal dose;

(xix) less than 8 % of the maximal dose;

(xx) less than 7 % of the maximal dose;

(xxi) less than 6 % of the maximal dose;

(xxii) less than 5 % of the maximal dose;

(xxiii) less than 4 % of the maximal dose;

(xxiv) less than 3 % of the maximal dose;

(xxv) less than 2 % of the maximal dose;

(xxvi) less than 1 % of the maximal dose;

(xxvii) less than 0.9 % of the maximal dose;

(xxviii) less than 0.8 % of the maximal dose;

(xxix) less than 0.7 % of the maximal dose;

(xxx) less than 0.6 % of the maximal dose;

(xxxi) less than 0.5 % of the maximal dose;

(xxxii) less than 0.4 % of the maximal dose;

(xxxiii) less than 0.3 % of the maximal dose;

(xxxiv) less than 0.2 % of the maximal dose;

(xxxv) less than 0.1 % of the maximal dose;

(xxxvi) less than 0.05 % of the maximal dose; or

(xxxvii) less than 0.01 % of the maximal dose;

According to yet another aspect of the present invention there is provided a method of radioimaging a region of interest in a subject, the method comprising:

(a) administering to the subject the composition of matter of any of claims 273 to 277; and

(b) using a high sensitivity radioactive-emission camera for collecting radioactive-emission data from the subject, thereby radioimaging the region of interest in the subject.

According to further features in preferred embodiments of the invention described below the high sensitivity is selected from the group consisting of:

(a) sensitivity in terms of speed of data collection and spatial resolution, at least as good as a gold standard for PET imaging for at rest myocardial perfusion with N-13-ammonia (NH_3), at a dose of 740 MBq with attenuation correction;

(b) sensitivity sufficient for reconstructing an image under a Cobalt wire Nema test of a line source of 5 mCi cobalt with a line spread function of less than 7 mm Full Width Half Maximum (FWHM) through air at a distance of at least 100 mm;

(c) sensitivity sufficient for resolving through air at a distance of at least 100 mm under a Nema Bar Phantom test of gaps formed between 1 mm wide led bars positioned less than 7 mm apart from one another over a uniform cobalt disc;

(d) sensitivity operative for image acquisition of a full organ in less than 10 seconds at a spatial resolution, capable of identifying objects not greater than about 7 mm X 7 mm X 7 mm with a signal-to-noise ratio of at least 4 to 1 or better; and/or

(e) sensitivity allowing aquizition of at least 1 out of every 5000 emmited photons while allowing a reconstructions of a 3D image with a resolution of not more than 5 mm and enery resolution of not more than 15 %.

According to further features in preferred embodiments of the invention described below the sensitivity is selected from the group consisting of:

at least 2 fold that of the gold standard for PET imaging;
at least 3 fold that of the gold standard for PET imaging;
at least 4 fold that of the gold standard for PET imaging;
at least 5 fold that of the gold standard for PET imaging;
at least 6 fold that of the gold standard for PET imaging;
at least 7 fold that of the gold standard for PET imaging;
at least 8 fold that of the gold standard for PET imaging;
at least 9 fold that of the gold standard for PET imaging;
at least 10 fold that of the gold standard for PET imaging;
at least 20 fold that of the gold standard for PET imaging;
at least 30 fold that of the gold standard for PET imaging;
at least 50 fold that of the gold standard for PET imaging;
at least 100 fold that of the gold standard for PET imaging;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of less than 6 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of less than 5 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of less than 4 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of less than 3 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of less than 2 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of the line source of 5 mCi cobalt with a line spread function of about 1 mm Full Width Half Maximum (FWHM) through air at the distance of at least 100 mm;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 6 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 5 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 4 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 3 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 2 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 1 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 0.5 mm apart from one another over the uniform cobalt disc;

sufficient for resolving through air at the distance of at least 100 mm under the Nema Bar Phantom test of the gaps formed between the 1 mm wide led bars positioned less than 0.1 mm apart from one another over the uniform cobalt disc;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 6 mm X 6 mm X 6 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 5 mm X 5 mm X 5 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 4 mm X 4 mm X 4 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 3 mm X 3 mm X 3 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 2 mm X 2 mm X 2 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 1 mm X 1 mm X 1 mm with the signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 0.5 mm X 0.5 mm X 0.5 mm with the signal-to-noise ratio of at least 4 to 1 or better; and/or

operative for image acquisition of the full organ in less than 10 seconds at the spatial resolution, capable of identifying objects not greater than about 0.1 mm X 0.1 mm X 0.1 mm with the signal-to-noise ratio of at least 4 to 1 or better.

According to yet another aspect of the present invention there is provided a method of packaging the composition-of matter of any of claims 273 to 277, the method comprising placing the low dose of the at least one radiopharmaceutical intended for the administration in whole to the human subject of the particular age and/or weight in a container or a syringe.

According to yet another aspect of the present invention there is provided a method of manufacturing the composition-of matter of any of claims 273 to 277, the method comprising generating the at least one radiopharmaceuticalnd collecting the at least one radiopharmaceutical at a time needed for having the low dose.

According to yet another aspect of the present invention there is provided a method of radioimaging comprising:

(a) administering to a human subject a low dose of a first radiopharmaceutical; and

(b) acquiring data representing a distribution of the first radiopharmaceutical in at least a section of the body of the subject during at least one time window.

According to yet another aspect of the present invention there is provided a method of radioimaging comprising:

(a) administering to a human subject a low dose of a first radiopharmaceutical; and

(b) acquiring data representing a distribution of the first radiopharmaceutical in at least a section of the body of the subject during at least one short time window.

According to further features in preferred embodiments of the invention described below the section of a body comprises the heart.

According to further features in preferred embodiments of the invention described below the method further comprises:

(c) subjecting the human subject to stress following the administering of the first radiopharmaceutical; and

(d) administering to the human subject a dose of at least a second radiopharmaceutical, prior to acquiring the data.

According to further features in preferred embodiments of the invention described below the method further comprises acquiring from the subject data representing a distribution of the first radiopharmaceutical in the subject during at least one short time window prior to subjecting the human subject to the stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi).

According to further features in preferred embodiments of the invention described below the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi.

According to further features in preferred embodiments of the invention described below the second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 8 to about 10 mCi.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi.

According to further features in preferred embodiments of the invention described below the short time window is not greater than about 6 minutes.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi and the short window time is not greater than about 4 minutes.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi and the short time window is not greater than about 4 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the first radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the second radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below a time period of from about 10 to about 15 minutes is allowed to elapse between the administering of the first radiopharmaceutical and the acquiring of data representing a distribution of the first pharmaceutical.

According to further features in preferred embodiments of the invention described below a time period from about 30 to about 60 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the second pharmaceutical.

According to further features in preferred embodiments of the invention described below a time period of from about 2 minutes is allowed to elapse between the administering of the first radiopharmaceutical and the acquiring of data representing a distribution of the first pharmaceutical.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second pharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises exercise stress.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 8 to about 10 mCi, the second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi and the short time window is not greater than about 4 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the first radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the second radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below a time period of about 30 minutes is allowed to elapse between the administering of the first radiopharmaceutical and the acquiring of data representing a distribution of the first pharmaceutical.

According to further features in preferred embodiments of the invention described below a time period from about 30 to about 60 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the second pharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises exercise stress.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the first pharmaceutical is performed immediately following administering of the first radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second pharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi, the second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, and the short time window is not greater than about 6 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the first radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the second radiopharmaceutical in the subject is acquired during a short time window of up to about 4 minutes.

According to further features in preferred embodiments of the invention described below a time period of about 30 minutes is allowed to elapse between the administering of the first radiopharmaceutical and the acquiring of data representing a distribution of the first pharmaceutical.

According to further features in preferred embodiments of the invention described below a time period from about 10 to about 15 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the second pharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises exercise stress.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second pharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the first pharmaceutical is performed immediately following administering of the first radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second pharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi)at a dose of from about 20 to about 30 mCi, and the short time window is not greater than about 2 minutes.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the first

radiopharmaceutical and the acquiring of data representing a distribution of second radiopharmaceutical are performed simultaneously.

According to further features in preferred embodiments of the invention described below a time period of from about 30 to about 60 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the first and the second radiopharmaceuticals.

According to further features in preferred embodiments of the invention described below the stress comprises exercise stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi, the second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, and the short time window is not greater than about 4 minutes.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the first radiopharmaceutical and the acquiring of data representing a distribution of second radiopharmaceutical are performed simultaneously.

According to further features in preferred embodiments of the invention described below a time period of from about 2 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the first and the second radiopharmaceuticals.

According to further features in preferred embodiments of the invention described below the section of a body comprises the lung.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises a combination of Tc-99m-diethylene triamine pentaacetate (DTPA), Tc-99m-macro-aggregated albumin, and iodine-123.

According to further features in preferred embodiments of the invention described below a concentration of the Tc-99m-macro-aggregated albumin is up to about 5 mCi.

According to further features in preferred embodiments of the invention described below the acquiring of data is performed immediately following administering of the first radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the section of a body comprises the bones.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises Tc-99m-disodium dihydrogen methylenediphosphate at a dose of from about 20 to about 30 mCi.

According to further features in preferred embodiments of the invention described below a time period of up to about 60 minutes is allowed to elapse between the administering of the radiopharmaceutical and the acquiring of data, and wherein , wherein the acquiring of data is performed at an energy window of from about 3 to about 15 percent.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-teboroxime at a dose of from about 8 to about 10 mCi, the second radiopharmaceutical comprises technetium-99m- teboroxime at a dose of from about 20 to about 30 mCi and the short time window is not greater than about 4 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the first radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the second radiopharmaceutical in the subject is acquired during a short time window of up to about 2 minutes.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the first pharmaceutical is performed immediately following administering of the first radiopharmaceutical.

According to further features in preferred embodiments of the invention described below a time period of about 10 minutes is allowed to elapse between the acquiring of data representing a distribution of the first pharmaceutical and the subjecting to the stress.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second

pharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the section of a body comprises the heart.

According to further features in preferred embodiments of the invention described below the method further comprises:

(c) subjecting the human subject to stress following the administering of the first radiopharmaceutical; and

(d) administering to the human subject a low dose of at least a second radiopharmaceutical, prior to acquiring the data.

According to further features in preferred embodiments of the invention described below the method further comprises acquiring from the subject data representing a distribution of the first radiopharmaceutical in the subject during at least one time window prior to subjecting the human subject to the stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi.

According to further features in preferred embodiments of the invention described below the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose about 3 mCi.

According to further features in preferred embodiments of the invention described below the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose about 30 mCi.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the first radiopharmaceutical in the subject is acquired during a time window of about 15 minutes.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the second

radiopharmaceutical in the subject is acquired during a time window of about 15 minutes.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 201 at a dose of about 0.3 mCi, and wherein the data representing a distribution of the second radiopharmaceutical in the subject is acquired during a time window of about 2 minutes

According to further features in preferred embodiments of the invention described below a time period from about 30 to about 60 minutes is allowed to elapse between the administering of the second radiopharmaceutical and the acquiring of data representing a distribution of the second pharmaceutical.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, and wherein a time period from about 10 to about 15 minutes is allowed to elapse between the administering of the thallium-201 and the acquiring of data representing a distribution of the thallium-201.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi, and wherein a time period from about 30 minutes is allowed to elapse between the administering of technetium-99m- methoxyisobutylisonitrile (sestamibi) and the acquiring of data representing a distribution of technetium-99m- methoxyisobutylisonitrile (sestamibi).

According to further features in preferred embodiments of the invention described below the stress comprises exercise stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, and wherein a time period of about 2 minutes is allowed to elapse between the administering of the thallium-201 and the acquiring of data representing a distribution of the thallium-201.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi, and wherein the

acquiring of data representing a distribution of the first radiopharmaceutical is performed immediately following administering of the first radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the acquiring of data representing a distribution of the second radiopharmaceutical is performed immediately following administering of the second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the stress comprises pharmacological stress.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, the second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi)at a dose of from about 3 to about 5 mCi, and wherein the acquiring of data representing a distribution of the thallium-201 and the technetium-99m- methoxyisobutylisonitrile (sestamibi) is performed simultaneously.

According to further features in preferred embodiments of the invention described below the data representing a distribution of the thallium-201 and the technetium-99m- methoxyisobutylisonitrile (sestamibi) in the subject is acquired during a time window of from about 5 to about 15 minutes.

According to further features in preferred embodiments of the invention described below a time period of from about 30 to about 60 minutes is allowed to elapse between the administering of technetium-99m- methoxyisobutylisonitrile (sestamibi) and the acquiring of data representing a distribution of the thallium-201 and the technetium-99m- methoxyisobutylisonitrile (sestamibi).

According to further features in preferred embodiments of the invention described below the acquiring of data is performed at an energy window of from about 3 to about 15 percent.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises thallium-201 at a dose of up to about 4 mCi, and the time window is from about 2 to about 20 minutes.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical is selected from the group consisting of Tc-99m-teboroxime, Tc-99m- methoxyisobutylisonitrile (sestamibi), Tc-99m-

tetrofosmin, Tc-99m-furifosmin (Q12), and Tc-99m-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP).

According to further features in preferred embodiments of the invention described below a dose of the first radiopharmaceutical is up to about 30 mCi, and the time window is up to about 15 minutes.

According to further features in preferred embodiments of the invention described below the subject is subjected to stress prior to acquiring of the data.

According to further features in preferred embodiments of the invention described below the methods are applied to cardiac perfusion studies.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical is Tc-99m- methoxyisobutylisonitrile (sestamibi), applied to tumor imaging.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is a combination of thallium-201 at a dose of up to 4 mCi and Tc-99m- methoxyisobutylisonitrile (sestamibi) at a dose of up to about 30 mCi, applied to tumor imaging.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is a combination of In-111-diethylene triamine pentaacetate (DTPA) at a dose of 0.2 mCi and Tc-99m-mercaptoacetyltriglycine (MAG3) at a dose of up to about 10 mCi, and the section of the body is the kidney.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is a combination of In-111-diethylene triamine pentaacetate (DTPA) at a dose of from about 0.3 to about 1 mCi and I-123-iodohippurate sodium (hippuran) at a dose of up to about 10 mCi, and the section of the body is the kidney.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is Tc-99m at a dose of up to about 5 mCi, applied to brain perfusion mapping.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is a combination of Tc-99m-Exametazine (HMPAO) at a dose of up to about 20 mCi, Tc-99m N,N'(1,2-ethlenediyl)bis-L-cysteine diethyl ester (Tc-99m ECD) at a dose of up to about 20 mCi, and I-123

iofetamine hydrochloride, at a dose of up to about 5 mCi, applied to brain perfusion mapping.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical is a combination of

Tc-99m-diisopropyl iminodiacetic acid (disulfenine), Tc-99m-2,2'-[[2-[(3-bromo-2,4,6-trimethylphenyl)-amino]-2-oxoethyl] imino] bisacetic acid (Tc-99m-mebrofenin), and Tc-99m-dimethyl iminodiacetic acid (HIDA), applied to liver function study.

According to further features in preferred embodiments of the invention described below the data is acquired immediately following administering of the first radiopharmaceutical at an energy window of from about 3 to about 15 percent.

According to further features in preferred embodiments of the invention described below the methods are applied to dynamic process imaging.

According to further features in preferred embodiments of the invention described below the methods are applied to the study of ventricular function study.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical comprises a combination of Tc-99m-colloid and In-111-diethylene triamine pentaacetate (DTPA), applied to the study of dual phase gastric emptying.

According to yet another aspect of the present invention there is provided a method of radioimaging comprising:

(a) administering to a human subject a dose of the composition of any of claims 350 to352; and

(b) acquiring data representing a distribution of each of the radiopharmaceutical of the composition in at least a section of the body of the subject.

According to yet another aspect of the present invention there is provided a composition comprising a first radiopharmaceutical and a second radiopharmaceutical being different from the first radiopharmaceutical, provided that if the fist radiopharmaceutical is Tc-99m the second radiopharmaceutical is not Thalium 201 and vice versa.

According to further features in preferred embodiments of the invention described below both the first and the second radiopharmaceuticals are at low doses.

According to yet another aspect of the present invention there is provided a low dose of a first radiopharmaceutical and a low dose of a second radiopharmaceutical being different from the first radiopharmaceutical.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and

Tc-99m-pertechnetate.

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 1 mCi and a dose of the Tc-99m-pertechnetate is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m- methoxyisobutylisonitrile (sestamibi); and

I-123.

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m- methoxyisobutylisonitrile (sestamibi) is about 15 mCi and a dose of the I-123 is up to about 100 μCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

I-123: and

Tc-99m- red blood cells or Tc-99m-dihygrogen methylenediphosphate (medronate).

According to further features in preferred embodiments of the invention described below the dose of the I-123 is about 4 mCi, a dose of the Tc-99m- red blood cells is up to about 10 mCi and a dose of the Tc-99m-dihygrogen methylenediphosphate (medronate) is up to about 10 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

In-111-L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[2-hydroxy-1-(hydroxy-methyl) propyl]-, cyclic 7)-disulfide (In-111-octreotide); and

Tc-99m-dihygrogen methylenediphosphate (medronate).

According to further features in preferred embodiments of the invention described below the dose of the In-111-octreotide is up to about 3 mCi and a dose of the Tc-99m- medronate is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

In-111-capromab pendetide; and

Tc-99m-red blood cells.

According to further features in preferred embodiments of the invention described below the dose of the In-111-capromab pendetide is of up to about 2 mCi and a dose of the Tc-99m-red blood cells is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m-colloid; and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m-colloid is up to about 15 mCi and a dose of the In-111-white blood cells is up to about 3 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and

Tc-99m-dihygrogen methylenediphosphate (medronate).

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 2 mC and a dose of the Tc-99m-dihygrogen methylenediphosphate (medronate) is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride;

'Te-99-m- methoxyisobutylisonitrile (sestamibi); and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 1 mCi, a dose of the Te-99-m- methoxyisobutylisonitrile (sestamibi) is up to about 10 mCi, and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride;

dihygrogen methylenediphosphate (medronate); and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 1 mCi, a dose of the dihygrogen methylenediphosphate (medronate) is up to about 10 mCi, and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride;

Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi); and

I-123-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP).

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi) is up to 10 mCi, and a dose of the I-123-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP) is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m-Fanoselomab; and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the a dose of the Tc-99m-Fanoselomab is up to about 15 mCi and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

I-123-iodobenzamide (IBZM); and

Tc-99m-Exametazine (HMPAO).

According to further features in preferred embodiments of the invention described below the dose of the I-123-iodobenzamide (IBZM) is up to about 2 mCi and a dose of the Tc-99m-Exametazine (HMPAO) is about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

In-111-labeled antibody;

Tc-99m- methoxyisobutylisonitrile (sestamibi) or Tc-99m- Arcitumomab; and

Tl-201-thallous chloride.

According to further features in preferred embodiments of the invention described below the dose of the In-111-labeled antibody is up to about 1 mCi, a dose of the Tc-99m- methoxyisobutylisonitrile (sestamibi) or Tc-99m-Arcitumomab is up to about 10 mCi and a dose of the Tl-201-thallous chloride is up to about 1 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

In-111-diethylene triamine pentaacetate (DTPA); and

Tc-99m-mercaptoacetyltriglycine (MAG3).

According to further features in preferred embodiments of the invention described below the dose of the In-111-diethylene triamine pentaacetate (DTPA) is up to about 2 mCi and a dose of the Tc-99m-mercaptoacetyltriglycine (MAG3) is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and

Tc-99m-teboroxime or Tc-99m- methoxyisobutylisonitrile (sestamibi).

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 1 mCi and a dose of the Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi) is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m-sulfur colloid; and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m-sulfur colloid is up to about 15 mCi and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m-dihygrogen methylenediphosphate (medronate); and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m-dihygrogen methylenediphosphate (medronate) is up to about 15 mCi and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

gallium-67; and

In-111-white blood cells.

According to further features in preferred embodiments of the invention described below the dose of the gallium-67 is up to about 5 mCi and a dose of the In-111-white blood cells is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tc-99m-teboroxime Tl-201-thallous chloride; and

In-111-annexin.

According to further features in preferred embodiments of the invention described below the dose of the Tc-99m-teboroxime is up to about 15 mCi, a dose of the Tl-201-thallous chloride is up to about 2 mCi, and a dose of the In-111-annexin is up to about 2 mCi.

According to yet another aspect of the present invention there is provided a kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein the at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and

Tc-99m-pyrophosphate.

According to further features in preferred embodiments of the invention described below the dose of the Tl-201-thallous chloride is up to about 2 mCi and a dose of the Tc-99m-pyrophosphate is up to about 15 mCi.

According to yet another aspect of the present invention there is provided a use of F-18-Fluorodeoxyglucose (FDG), as a substrate for hexokinase in glucose metabolism, for the study of glucose metabolism of cells including tumor, heart and brain cells.

According to yet another aspect of the present invention there is provided a use of F-18-Fluoromisonidazole for imaging of hypoxia and oxidative metabolism, with the clinical application of radiotherapy treatment planning.

According to yet another aspect of the present invention there is provided a use of F-18-3'-Fluoro-3'-deoxythymidine (FLT) for the study of DNA synthesis.

According to yet another aspect of the present invention there is provided a use of F-18-Fluoromethyl choline (FCH) as a choline precursor for cell membrane synthesis, for the study of choline metabolism of tumors.

According to yet another aspect of the present invention there is provided a use of F-18-4-Fluoro-m-tyrosine (FMT) as a precursor for dopamine synthesis and as a substrate for aromatic amino acid decarboxylase (AAAD), with the clinical application of imaging brain tumors.

According to yet another aspect of the present invention there is provided a use of F-18-6-Fluoro-L-DOPA as a precursor for dopamine synthesis and as a precursor for AAAD, with the clinical applications of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

According to yet another aspect of the present invention there is provided a use of F-18-FP-β-CIT for binding to the dopamine transporter in dopaminergic axons, with the clinical application of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

According to yet another aspect of the present invention there is provided a use of F-18-Pencyclovir (FHBG) to target thymidine kinase, with the clinical application of imaging reporter gene expression.

According to yet another aspect of the present invention there is provided a use of F-18-Fuoroestradiol (FES) to target estrogen receptors, with the clinical application of breast tumor imaging.

According to yet another aspect of the present invention there is provided a use of C-11-Methionine to target amino acid synthesis, with the clinical application of imaging brain tumors.

According to yet another aspect of the present invention there is provided a use of Tc-99m-P280, Acutect® to target GP IIb/IIIa receptors on platelets, with the clinical applications of detection of thrombosis, such as deep vein thrombosis (DVT) and intratererial thrombosis in coronary and carotid arteries.

According to yet another aspect of the present invention there is provided a use of C-11-Raclopride to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

According to yet another aspect of the present invention there is provided a use of I-123-iodobenzamide (IBZM) to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

According to yet another aspect of the present invention there is provided a use of C-11-carfentanil to target Mu opioid receptors in brain, with the clinical application of imaging drug addiction.

According to yet another aspect of the present invention there is provided a use of C-11-α-methyl-L-tryptophan as a precursor for α-methyl serotonin synthesis and as a substrate for AAAD enzyme, with the clinical application of imaging depression.

According to yet another aspect of the present invention there is provided a use of C-115-Hydroxytryptophan as a precursor for serotonin synthesis with the clinical application of imaging neuroendocrine tumors.

According to yet another aspect of the present invention there is provided a use of F-18-MPPF to bind to 5-HT1A (5-hydroxytryptamine-1A) serotonin receptors, with the clinical application of imaging depression and epilepsy.

According to yet another aspect of the present invention there is provided a use of F-18-Altanserin to bind to 5-HT2A serotonin receptors with the clinical application of imaging depression and epilepsy.

According to yet another aspect of the present invention there is provided a use of C-11-Acetate for the study of tricarboxylic acid cycle activity and oxidative metabolism with the clinical application of studying myocardial oxygen metabolism.

According to yet another aspect of the present invention there is provided a use of C-11-Palmitate as a precursor for fatty acid metabolism with the clinical application of imaging myocardial metabolism.

According to yet another aspect of the present invention there is provided a use of F-18-Fluorodopamine to target presynaptic adrenergic receptors.

According to yet another aspect of the present invention there is provided a method for treating a patient, comprising:

(a) applying a therapy to the patient;

(b) performing on the patient a functional imaging procedure according to a method of any of claims 1-385 to measure a property indicative of biochemical activity of at least one tissue of the patient; and

modifying at least one parameter of the therapy responsively to the measured biochemical activity.

According to further features in preferred embodiments of the invention described below performing the imaging procedure comprises performing a SPECT imaging procedure on the patient.

According to further features in preferred embodiments of the invention described below the performing the SPECT imaging procedure comprises performing the SPECT imaging procedure using a high-definition SPECT camera.

According to further features in preferred embodiments of the invention described below the therapy comprises a therapeutic radiopharmaceutical.

According to yet another aspect of the present invention there is provided an apparatus for use with any of the methods, kits and compositions of claims 1-428, the apparatus comprising:

a container containing at least one radiopharmaceutical of the methods, kits or compositions of claims 1-428; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information of any of the methods of claims 1-385 for use with the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

According to further features in preferred embodiments of the invention described below the data carrier additionally contains administration protocol information useful for administering the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises instructions for performing an imaging procedure using the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises an identifier of an imaging protocol.

According to further features in preferred embodiments of the invention described below the the imaging protocol information comprises a parameter of the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises a parameter useful for

configuring at least one aspect of an imaging procedure performed using the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information.

According to further features in preferred embodiments of the invention described below the container contains a plurality of radiopharmaceuticals mixed together.

According to further features in preferred embodiments of the invention described below the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of radiopharmaceuticals.

According to further features in preferred embodiments of the invention described below the data carrier comprises a first data carrier, which contains a first identifier value,

wherein the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and

wherein the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values.

According to further features in preferred embodiments of the invention described below at least one of the first and second data carriers is configured to perform the detection of the correspondence.

According to further features in preferred embodiments of the invention described below the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

According to further features in preferred embodiments of the invention described below at least one of the first and second data carriers contains an identifier of a patient to whom the radiopharmaceutical is to be administered.

According to further features in preferred embodiments of the invention described below at least one of the first and second identifier values comprises an identifier of a patient to whom the radiopharmaceutical is to be administered.

According to further features in preferred embodiments of the invention described below exactly one of the first and second data carriers comprises a coupling

mechanism configured to be coupled to a patient to whom the radiopharmaceutical is to be administered.

According to further features in preferred embodiments of the invention described below the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the data carrier is physically coupled to the container.

According to further features in preferred embodiments of the invention described below the data carrier contains an identifier of a patient to whom the radiopharmaceutical is to be administered, and wherein the imaging protocol information comprises imaging protocol information selected for the patient.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises an identifier of an imaging protocol.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises imaging protocol information customized for the patient.

According to further features in preferred embodiments of the invention described below the the imaging protocol information comprises SPECT imaging protocol information.

According to further features in preferred embodiments of the invention described below the SPECT imaging protocol information comprises dynamic SPECT imaging protocol information.

According to further features in preferred embodiments of the invention described below the SPECT imaging protocol information comprises at least one kinetic parameter of the at least one radiopharmaceutical, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the imaging protocol information from the data carrier; and

a control unit, comprising imaging functionality, which is configured to perform an imaging procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the imaging system comprises a camera, wherein the imaging functionality comprises image acquisition functionality, and wherein the image acquisition functionality is configured to perform an image acquisition procedure using the camera, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the image acquisition functionality configures a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

According to further features in preferred embodiments of the invention described below the camera comprises a plurality of detectors, and wherein the image acquisition functionality is configured to configure, at least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image acquisition procedure.

According to further features in preferred embodiments of the invention described below the control unit is configured to configure, at least in part responsively to the imaging protocol information, a waiting time between administration of the radiopharmaceutical and commencement of the image acquisition procedure.

According to further features in preferred embodiments of the invention described below the image acquisition functionality is configured to perform a gated image acquisition procedure at least in part responsively to the imaging protocol information.

According to further features in preferred embodiments of the invention described below the imaging functionality comprises image reconstruction functionality, and wherein the image reconstruction functionality is configured to perform an image reconstruction procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the imaging functionality comprises image analysis functionality, and wherein the image analysis functionality is configured to perform an image analysis procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the the imaging functionality comprises diagnosis functionality, and wherein the diagnosis functionality is configured to perform a diagnostic procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study, and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

According to further features in preferred embodiments of the invention described below the the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the radiopharmaceutical is to be administered.

According to further features in preferred embodiments of the invention described below the data carrier comprises a coupling mechanism configured to be coupled to the patient.

According to further features in preferred embodiments of the invention described below the data carrier comprises a first data carrier, and wherein the

apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the apparatus is for use with at least one radiopharmaceutical of any of the kits, compositions or methods of claims 1-428, the apparatus comprising:

a container containing the at least one radiopharmaceutical; and

a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of the imaging protocol information of any of the methods of claims 1-385 with the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the apparatus comprisesan imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

According to further features in preferred embodiments of the invention described below the data carrier is physically coupled to the container.

According to yet another aspect of the present invention, there is provided an apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of any of the imaging methods of claims 1-385.

According to further features in preferred embodiments of the invention described below the data carrier additionally contains patient information regarding a

patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

According to further features in preferred embodiments of the invention described below the authenticatable license information is encrypted.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

According to further features in preferred embodiments of the invention described below the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

According to further features in preferred embodiments of the invention described below the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

According to anothere aspect of the present invention, there is provided an pparatus for use with at least one radiopharmaceutical of the methods and kits of claims 1-385 and 389-428 for administration to a patient, the apparatus comprising:

a container containing the at least one radiopharmaceutical;

a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one radiopharmaceutical; and

a second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises SPECT imaging protocol information.

According to further features in preferred embodiments of the invention described below the patient information comprises an identifier of the patient.

According to further features in preferred embodiments of the invention described below the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

According to further features in preferred embodiments of the invention described below the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier comprises a second patient identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

a second communication element, configure to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

According to further features in preferred embodiments of the invention described below the the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

According to further features in preferred embodiments of the invention described below the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

According to further features in preferred embodiments of the invention described below the apparatus comprises an administration system, which comprises:

a communication element; and

a control unit, configured to:

generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container, and

drive the communication element to transmit information regarding the administration to the second data carrier.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the imaging protocol information to the first data carrier.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the patient information to the second data carrier.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises imaging protocol information selected for the patient.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises an identifier of an imaging protocol.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises imaging protocol information customized for the patient.

According to further features in preferred embodiments of the invention described below the first data carrier contains a first patient identifier, wherein the

patient information contained in the second data carrier includes a second patient identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

According to further features in preferred embodiments of the invention described below the administration system comprises an automated administration device, configured to administer the at least one radiopharmaceutical to the patient upon being triggered by the administration signal.

According to further features in preferred embodiments of the invention described below the control unit is configured to generate the administration signal to trigger the administration of the at least one radiopharmaceutical by instructing a healthcare worker to administer the at least one radiopharmaceutical to the patient.

According to further features in preferred embodiments of the invention described below the apparatus comprises:

a container containing the at least one radiopharmaceutical;

a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the radiopharmaceutical and the patient; and

a SPECT imaging system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the radiopharmaceutical, acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

According to further features in preferred embodiments of the invention described below the the data carrier contains the data regarding the radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the data carrier contains the data regarding the patient.

According to further features in preferred embodiments of the invention described below the control unit is configured to utilize the read data to customize the administration of the radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered.

According to further features in preferred embodiments of the invention described below the control unit is configured to utilize the read data to customize the reconstruction of the SPECT image.

According to further features in preferred embodiments of the invention described below the control unit is configured to utilize the read data to customize the analysis of the SPECT image.

According to further features in preferred embodiments of the invention described below the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

According to further features in preferred embodiments of the invention described below the apparatus comprises a device configured to write the data to the data carrier.

According to yet another aspect of the present invention there is provided a SPECT imaging system for use with a container containing at least one radiopharmaceutical for administration to a patient according to the method of any of claims 1-385, and data regarding at least one of: the radiopharmaceutical and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the radiopharmaceutical, acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

According to further features in preferred embodiments of the invention described below the system comprises a device configured to write the data to the container.

According to yet another aspect of the present invention, there is provided an automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container and for using of any of the kits of claims 389-428 and/or executing any of the methods of claims 1-385, the system comprising:

a robot, configured to manipulate the container;

a communication element; and

a control unit, configured to:

receive radiopharmaceutical information regarding at least one radiopharmaceutical, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one radiopharmaceutical, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one radiopharmaceutical,

receive patient information regarding a patient,

drive the robot to automatically dispense a dose of the radiopharmaceutical to the container, and

drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

According to further features in preferred embodiments of the invention described below the control unit is configured to receive the radiopharmaceutical information regarding a plurality of radiopharmaceuticals, and drive the robot to automatically dispense respective doses of the radiopharmaceuticals to the container.

According to further features in preferred embodiments of the invention described below the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

According to further features in preferred embodiments of the invention described below the control unit is configured to drive the communication element to

transmit to the container data carrier at least one of: a time of dispensing of the radiopharmaceutical to the container, and information regarding a radioactivity of the dose at the time of dispensing.

According to further features in preferred embodiments of the invention described below the system comprises:

a mother vial that contains the radiopharmaceutical prior to dispensing thereof; and

a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information,

wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

According to further features in preferred embodiments of the invention described below the the radiopharmaceutical information comprises the imaging protocol information.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises SPECT imaging protocol information.

According to further features in preferred embodiments of the invention described below the imaging protocol information comprises at least one kinetic parameter of the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the radiopharmaceutical information comprises the authenticatable information regarding the commercial license.

According to further features in preferred embodiments of the invention described below the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the control unit is configured to authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

According to yet another aspect of the present invention, there is provided an imaging system for implementing any of the methods or using any of the kits or compositions of claims 1-428, the imaging system comprising a radioimaging camera,

which comprises a plurality of solid state detectors, configured for independent movement during data acquisition.

According to yet another aspect of the present invention, there is provided an imaging system for implementing any of the methods of claims 1-385, or using any of the kits of claims 389-428 the system comprising a radioactive-emission-measuring-camera system which comprises:

a housing;

at least one detecting unit, located within the housing and adapted for at least one form of motion with respect to the housing;

at least one motion provider, in mechanical communication with the at least one detecting unit, for providing it with the at least one form of motion;

a controller, in signal communication with the at least one motion provider, for instructing it regarding the at least one form of motion of the at least one detecting unit, thus automatically providing the at least one detecting unit with the at least one form of motion.

According to further features in preferred embodiments of the invention described below the at least one detecting unit includes a plurality of detecting units, each detecting unit moving independently.

According to another aspect of the present invention there is provided a diagnostic pharmaceutical kit comprising

(i) a packaged dose unit of a first diagnostic radiopharmaceutical:

(ii) a packaged dose unit of a second diagnostic radiopharmaceutical;

(iii) a packaged dose unit of saline; and

(iv) a packaged dose unit of a pharmacological stress agent.

According to further features in preferred embodiments of the invention described below the pharmacological stress agent is selected from the group consisting of adenosine, dipyridamole or dobutamine.

According to further features in preferred embodiments of the invention described below the packaged dose unit of said first diagnostic radiopharmaceutical is a low dose.

According to further features in preferred embodiments of the invention described below the low dose is about 2.5 mrem or less per kg body weight.

According to further features in preferred embodiments of the invention described below the first diagnostic radiopharmaceutical is Tc99.

According to further features in preferred embodiments of the invention described below the low dose is less than 6 mCi.

According to further features in preferred embodiments of the invention described below the packaged dose unit of said second diagnostic radiopharmaceutical is a high dose.

According to further features in preferred embodiments of the invention described below the second diagnostic radiopharmaceutical is Tc99.

According to further features in preferred embodiments of the invention described below the high dose is between 25-50 mCi.

According to further features in preferred embodiments of the invention described below the high dose is about 30 mrem or more per kg body weight.

According to further features in preferred embodiments of the invention described below each of said packaged dose units are associated with a portable computer-communicatable data carrier, the data carrier containing imaging protocol information for use with said packaged dose units.

According to another aspect of the present invention, there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject a low dose of a first radiopharmaceutical;

(b) subjecting said subject to a physical stress;

(c) administering to said subject at a peak of said physical stress a medium or high dose of a second radiopharmaceutical;

(d) immediately radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical and said second radiopharmaceutical are identical.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical and said second radiopharmaceutical is Tc99.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical and said second radiopharmaceutical are not identical.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical is Tl201 and said second radiopharmaceutical is Tc99.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical is Tl201 and said second radiopharmaceutical is Iodine 123.

According to further features in preferred embodiments of the invention described below the first radiopharmaceutical is Tc99 and said second radiopharmaceutical is Iodine 123.

According to further features in preferred embodiments of the invention described below a length of time of steps a-d is no more than 20 minutes.

According to further features in preferred embodiments of the invention described below a length of time of steps a-d is no more than 30 minutes.

According to further features in preferred embodiments of the invention described below the method comprises only one radioimaging step.

According to further features in preferred embodiments of the invention described below the method further comprises radiomaging a heart of said subject following step (a).

According to further features in preferred embodiments of the invention described below the method takes less than 20 minutes.

According to further features in preferred embodiments of the invention described below the method takes less than 30 minutes.

According to further features in preferred embodiments of the invention described below the method is effected as described in Tables 91 or 92.

According to yet another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject a radiopharmaceutical;

(b) immediately radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below the length of time of steps a-b is no more than 10 minutes.

According to further features in preferred embodiments of the invention described below the radioimaging takes less than 6 minutes.

According to further features in preferred embodiments of the invention described below the radioimaging takes less than 3 minutes.

According to further features in preferred embodiments of the invention described below the radioimaging generates a 3D spectrum image and takes less than 6 minutes.

According to further features in preferred embodiments of the invention described below the radioimaging comprises generation of multiple images at multiple time points post injection.

According to further features in preferred embodiments of the invention described below the method is effected under the camera.

According to further features in preferred embodiments of the invention described below the multiple images generate information on turn-over kinetics.

According to further features in preferred embodiments of the invention described below the methods are controlled in accordance with an information carrier attached to a container of said first and said second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the administering if provided by an automatic injector which responds to a protocol information encrypted in said information carrier.

According to further features in preferred embodiments of the invention described below the methods further comprising administering to the subject a trace amount of radiopharmaceutical prior to step (a).

According to further features in preferred embodiments of the invention described below the trace amount is less than 2 mCi.

According to further features in preferred embodiments of the invention described below the trace amount is less than 1 mCi.

According to further features in preferred embodiments of the invention described below the method further comprises radioimaging an organ of interest following said administering said trace amount of radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the further radioimaging generates a baseline intensity image of said radiopharmaceutical existing in the body.

According to yet another aspect of the present invention there is provided a diagnostic pharmaceutical kit comprising

(i) a packaged dose unit of a first diagnostic radiopharmaceutical: and

(ii) a packaged dose unit of saline.

According to yet another aspect of the present invention there is provided a diagnostic pharmaceutical kit comprising

(i) a packaged dose unit of a first diagnostic radiopharmaceutical: and

(ii) a packaged dose unit of a pharmacological stress agent.

According to further features in preferred embodiments of the invention described below the kits further comprising a second radiopharmaceutical.

According to further features in preferred embodiments of the invention described below the kit further comprises a pharmacological stress agent.

According to further features in preferred embodiments of the invention described below the kit further comprises a packaged dose unit of saline.

According to further features in preferred embodiments of the invention described below each of said packaged dose units are associated with a portable computer-communicatable data carrier, the data carrier containing imaging protocol information for use with said packaged dose units.

The present invention successfully addresses the shortcomings of the presently known configurations by providing novel protocols for radioimaging.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Implementation of the method and system of the present invention involves performing or completing selected tasks or steps manually, automatically, or a combination thereof. Moreover, according to actual instrumentation and equipment

of preferred embodiments of the method and system of the present invention, several selected steps could be implemented by hardware or by software on any operating system of any firmware or a combination thereof. For example, as hardware, selected steps of the invention could be implemented as a chip or a circuit. As software, selected steps of the invention could be implemented as a plurality of software instructions being executed by a computer using any suitable operating system. In any case, selected steps of the method and system of the invention could be described as being performed by a data processor, such as a computing platform for executing a plurality of instructions.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

FIGS. 1A – 1B schematically illustrate detecting units and blocks for radioactive emission detection;

FIG. 2 schematically illustrates the basic component of a system, comprising a radioactive-emission camera and a position-tracking device, both in communication with a data-processing system;

FIGS. 3A – 3B schematically illustrate the manner of operating the radioactive-emission camera with the position-tracking device;

FIGS. 4A – 4C schematically illustrate extracorporeal and intracorporeal radioactive-emission camera operative with position-tracking devices;

FIGS. 5A – 5F present the principles of modeling, for obtaining an optimal set of views, in accordance with embodiments of the present invention;

FIGS. 6A and 6B pictorially illustrate a view and viewing parameters associated with it, in accordance with definitions of the present invention;

FIGS. 7A – 7C schematically illustrate anatomical constraints, which are to be modeled, in accordance with embodiments of the present invention;

FIG. 8 illustrates, in flowchart form, a method of predefining a set of views for functional imaging, tailored for imaging a specific body structure, and optimized with respect to the functional information gained about the body structure, in accordance with embodiments of the present invention;

FIGS. 9A – 9F schematically illustrate possible models and collections of views, for a body structure, in accordance with embodiments of the present invention;

FIG. 10 illustrates, in flowchart form, a method of functional imaging, tailored for imaging from esophagus, and optimized with respect to the functional information gained about the body structure, in accordance with embodiments of the present invention;

FIG. 11 schematically illustrates the process of modeling in two iterations, for zooming in on a pathological feature, in accordance with embodiments of the present invention;

FIG. 12 illustrates, in flowchart form, a method of several iterations for zooming in on a pathological feature, when performing in vivo measurements, in accordance with embodiments of the present invention;

FIGS. 13A – 13E schematically illustrate possible camera designs, and the process of obtaining views based on a model and a camera design, in accordance with embodiments of the present invention;

FIG. 14 illustrates, in flowchart form, a method of selecting a camera design optimized with respect to information gained about a body structure, in accordance with embodiments of the present invention;

FIG. 15 illustrates, in flowchart form, a method of selecting a camera design, based on the rate of data collection and other design considerations, in accordance with embodiments of the present invention;

FIGS. 16A – 16L schematically illustrate viewing of an elliptical modeled volume, by the radioactive-emission camera, in accordance with embodiments of the present invention;

FIGS. 17A – 17N schematically illustrate various detecting units and blocks, which may be incorporated in camera designs, in accordance with embodiments of the present invention;

FIGS. 18A – 18D schematically illustrate possible motions of a radioactive-emission camera, for a single detecting unit and a single block, in accordance with embodiments of the present invention;

FIGS. 19A – 19E schematically illustrate other possible motions of a radioactive-emission camera, for a single block, in accordance with embodiments of the present invention;

FIGS. 20A – 20H schematically illustrate possible motions of a radioactive-emission camera, having a plurality of pairs of radioactive-emission blocks;

FIGS. 21A – 21D schematically illustrate other possible motions of a radioactive-emission camera, having a plurality of pairs of radioactive-emission blocks;

FIGS. 22A – 22X schematically illustrate a radioactive-emission camera system, comprising a plurality of assemblies, motions of individual blocks, and characteristics of an optimal camera, in accordance with embodiments of the present invention;

FIG 22Y – 22AA schematically illustrate a center of viewing, for a given camera design, in accordance with embodiments of the present invention;

FIGS. 23A – 23D schematically illustrate a radioactive-emission camera system, in accordance with embodiments of the present invention;

FIGS. 24A – 24C schematically illustrate the modeling of a prostate as a process of two iterations, for zooming in on a pathology, in accordance with embodiments of the present invention;

FIGS. 25A – 25E schematically illustrate the external appearance and the internal structure of the radioactive-emission camera for the prostate, in accordance with an embodiment of the present invention;

FIG. 26 illustrates further the internal structure of the radioactive-emission camera for the prostate, in accordance with an embodiment of the present invention;

FIG. 27 schematically illustrates the radioactive-emission camera for the prostate, integrated with an ultrasound camera, in accordance with another embodiment of the present invention;

FIG. 28 schematically illustrates an ultrasound wave impinging on a prostate, in accordance with embodiments of the present invention;

FIGS. 29A - 29C illustrate the co-registering of a radioactive-emission image and an ultrasound image, in accordance with embodiments of the present invention;

FIG. 30 schematically illustrates the radioactive-emission camera for the prostate, integrated with a surgical needle, in accordance with another embodiment of the present invention;

FIGS. 31 and 32 schematically illustrates the operation of the surgical needle of FIG. 30; and

FIG. 33 schematically illustrates the modeling of the female reproductive system as a process of two iterations, for zooming in on a pathology, in accordance with embodiments of the present invention;

FIGS. 34A – 34R schematically illustrate the external appearance and the internal structure of the radioactive-emission camera for the female reproduction tract, in accordance with an embodiment of the present invention;

FIGS. 35A – 35Q schematically illustrate the external appearance and the internal structure of the radioactive-emission camera for the esophagus, in accordance with an embodiment of the present invention;

FIGS. 36A and 36B schematically illustrates body organs, including an esophagus.

FIGS. 37-39 schematically illustrate the modeling of the heart as a process of two iterations, in accordance with embodiments of the present invention;

FIGS. 40-45 schematically illustrate the basic components of a cardiac camera system, in accordance with an embodiment of the present invention;

FIG. 46 schematically illustrates the external appearance of a radioactive-emission-camera system for the heart, in accordance with an embodiment of the present invention;

FIGS. 47 and 48 schematically illustrate the internal structure of the radioactive-emission camera for the heart, in accordance with an embodiment of the present invention;

FIGS. 49A and 49B schematically illustrate the internal structure of the radioactive-emission camera for the heart, in accordance with an embodiment of the present invention;

FIG. 50 schematically illustrates the construction of radiation detection blocks, in accordance with an embodiment of the present invention;

FIG. 51 schematically illustrates a cardiac model, in accordance with an embodiment of the present invention;

FIGS. 52A-52E schematically illustrate radiation detection blocks arranged for viewing a cardiac model, in accordance with an embodiment of the present invention;

FIG. 53 schematically illustrates a dual imaging system for radioactive-emissions in tandem with a three-dimensional structural imager, in accordance with an embodiment of the present invention;

FIG. 54 schematically illustrates a dual imaging system for radioactive-emissions in tandem with a three-dimensional structural imager, in accordance with an embodiment of the present invention;

FIGS. 55A-55C schematically illustrate the internal structure of the radioactive-emission camera for the dual imaging system, in accordance with an embodiment of the present invention;

FIGS. 56A-56B schematically illustrate the internal structure of the radioactive-emission camera for the dual imaging system, in accordance with an embodiment of the present invention;

FIGS. 57A-57B schematically illustrate a cranial model, in accordance with an embodiment of the present invention;

FIG. 58 schematically illustrates a cranial model, in accordance with an embodiment of the present invention;

FIGS. 59A-59C schematically illustrate an imaging system for radioactive-emissions of the head, in accordance with an embodiment of the present invention;

FIGS. 60A-60K schematically illustrate the internal structure of the radioactive-emission camera for the head, in accordance with an embodiment of the present invention;

FIG. 61A and 61B schematically illustrate a breast model, in accordance with an embodiment of the present invention;

FIGS. 62A-62C schematically illustrate an imaging system for radioactive-emissions of the breast, in accordance with an embodiment of the present invention;

FIGS. 63A-63E schematically illustrate an imaging camera for radioactive-emissions of the breast, in accordance with an embodiment of the present invention;

FIGS. 64A-64K schematically illustrate an imaging system for radioactive-emissions of the breast, in accordance with an embodiment of the present invention;

FIGS. 64L-64M illustrates, in flowchart form, a method of examining a breast, in accordance with embodiments of the present invention;

FIGS. 65A-65C schematically illustrate an imaging camera for radioactive-emissions of the breast, in accordance with an embodiment of the present invention;

FIGS. 66A-66G schematically illustrate an imaging system for radioactive-emissions of the breast, in accordance with an embodiment of the present invention;

FIGS. 67A-67B schematically illustrate effect of distance on detection efficiency of a radiation detector;

FIGS. 68A-68D schematically illustrate effect of distance on resolution of a radiation detector;

FIGS. 69A-69D schematically illustrate "wasteful viewing" by an array of radiation detectors;

FIGS. 70A – 70C describe experimental results with grid point sources.

FIGS. 71 schematically illustrates a non-wasteful radiation detector array, in accordance with an embodiment of the present invention;

FIGS. 72A-72E schematically illustrate non-wasteful radiation detector arrays, in accordance with an embodiment of the present invention;

FIGS. 73A and 73B schematically illustrate non-wasteful radiation detector arrays, in accordance with an embodiment of the present invention;

FIGS. 74A and 74B schematically illustrate the use of a non-wasteful radiation detector array, in accordance with an embodiment of the present invention;

FIG. 75A and 75B illustrate Teboroxime physiological behavior, according to Garcia et al. (Am. J. Cardiol. 51st Annual Scientific Session, 2002).

FIGS. 76A – 80D schematically illustrate experimental data with the camera of the present invention.

FIG. 81 is a description of advantageous and disadvantageous viewing positions according to embodiments of the present invention.

FIG. 82 is a simplified flowchart of a method of performing radioactive-emission measurements of a body structure, according to a preferred embodiment of the present invention.

FIG. 83 shows an object shaped as a cylinder with a front protrusion, and having a high-remittance portion (hotspot).

FIG. 84a illustrates an object having two high-emission regions of interest.

FIG. 84b illustrates the added information provided by each of views V_A to V_F.

FIGS. 85a and 85b are simplified flowcharts of iterative methods of performing radioactive-emission measurements of a body structure, according to a first and a second preferred embodiment of the present invention.

FIGS. 86a and 86b are simplified flowcharts of methods for dynamically defining further views, according to a first and a second preferred embodiment of the present invention.

FIG. 87 is a simplified flowchart of an iterative method for selecting further views, according to a preferred embodiment of the present invention.

FIG. 88 is a simplified flowchart of a single iteration of a view selection method, according to a preferred embodiment of the present invention.

FIG. 89 is a simplified flowchart of a method for dynamically defining further views, according to a third preferred embodiment of the present invention.

FIG. 90 is a simplified block diagram of measurement unit for performing radioactive-emission measurements of a body structure, according to a preferred embodiment of the present invention.

FIG. 91 is a simplified flowchart of a method for measuring kinetic parameters of a radiopharmaceutical in a body, according to a preferred embodiment of the present invention.

FIG. 92 is a schematic representation of a dynamic model of a voxel, according to a first preferred embodiment of the present invention.

FIG. 93 is a schematic representation of a dynamic model of a voxel, according to a second preferred embodiment of the present invention.

FIG. 94 is a schematic representation of a dynamic model of a voxel, according to a third preferred embodiment of the present invention.

FIG. 95 is a circuit diagram of a series RLC electronic circuit.

FIG. 96 is a simplified flowchart of a method for measuring kinetic parameters of a radiopharmaceutical in an organ of a body, according to a preferred embodiment of the present invention.

FIG. 97 is a simplified flowchart of a process for obtaining the drug formulation, according to a preferred embodiment of the present invention.

FIG. 98 is a tabulation of events collected at temporal resolution of 1 ms in accordance with an embodiment of the present invention.

FIG. 99 A-E are tables showing exemplary preconfigured SPECT protocols and parameters thereof, in accordance with respective embodiments of the present invention;

FIG. 100 is a schematic illustration of an end-to-end automated system 10 for medical imaging, in accordance with an embodiment of the present invention. System 10 comprises a plurality of integrated elements that are configured to electronically exchange information among one another. The elements include an automated radiopharmaceutical dispensing system 20, a portable information-bearing radiopharmaceutical agent container 22, a portable patient-specific data carrier 24, an automated administration system 26, and an automated imaging system 28. Other exemplary components are indicated in the figure and further described hereinbelow.

The systems perform their respective automated functions at least in part responsively to the exchanged information. The elements typically authenticate one another via the exchanged information, in order to ensure that only authorized elements participate in the system, and that only authorized and appropriate functions are performed. Each of the elements is described in detail hereinbelow.

FIGs. 101A – 101H are experimental results, in accordance with embodiments of the present invention.

FIG. 102A-B are angiographic results of a 47 year old male, BMI 25 with a family history of premature CAD and atypical chest pain as detected using the camera in accordance with embodiments of the present invention (Figure 102B) and a standard SPECT camera (Figure 102A). Angiographic results: ostium circumflex 80 % and distal circumflex 80 % stenosis; LAD: mid 70 % stenosis. Ischemia in LCX territory (arrows) detected by the camera in accordance with embodiments of the present invention and not by conventional SPECT about an hour later.

FIGs. 103A-B are angiographic results using single (^{201}Tl) and dual isotope (^{201}Tl+^{99m}Tc) SPECT of a 1 cm lesion in the anterior myocardial wall. Note the blurring and diminishing of the lesion in the lower row on the conventional SPECT when imaged under the influence of the ^{99m}Tc crosstalk. This image degradation is

almost not perceivable on the images by analysis according to an embodiment of the present invention predicting preserved lesion detection capability even under simultaneous dual isotope SPECT imaging.

FIGs. 104A-B compare perfusion defect (2cm cold insert) from Tl-201 images obtained with simultaneous dual isotope acquisition to "virgin" Tl-201 acquisition.

FIGs.105-106 describe the experimental set up using the camera according to embodiments of the present invention (D-SPECT; Figure 105) and a standard camera (GE Millenium; Figure 106).

FIGs. 107A-B - 110A-B are further results of the torso phantom dual isotope study.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention relates to novel radioimaging protocols which may be used for the visualization of specific tissues or regions of the body.

The principles and operation of the novel protocols according to the present invention may be better understood with reference to the accompanying description.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

The following is a list of terminology related to the protocols of the present invention:

Terminology

As used herein a "subject" refers to a mammal, preferably a human subject.

As used herein the term "rest" refers to a non-exertion of physical activity for a period of time between the injection of the radio-isotope and acquisition of a resting scan.

As used herein the term "waiting" refers to the period of time between the injection and acquisition during which a subject is not engaged in a particular overt behavior. Typically the waiting period is to allow for distribution of the radioisotope in the body and clearance from organs such as the liver. The scan which is imaged following this period may be a resting scan or a stress scan.

As used herein the phrase "physical stress" refers to any physical activity which results in dilation of the blood vessels to the heart. Typically, the physical stress is an exercise treadmill.

As used herein the phrase "pharmacological stress" refers to any agent which results in dilation of the blood vessels to the heart. Examples of pharmacological stress include but are not limited to administration of adenosine, dipyridamole or dobutamine. Typically, the pharmacological stress is adenosine or dipyridamole.

As used herein the phrase "peak physical stress" refers to a safe amount of physical stress that will cause a sufficient vasodilation for myocardial perfusion imaging. Thus, the peak physical stress depends on patient parameters such as, but not limited to BMI, sex and medical conditions, as further described hereinbelow.

As used herein the phrase "peak pharmacological stress" refers to an amount of vasodilation exerted by an agent, sufficient for myocardial perfusion imaging. The peak pharmacological stress depends on patient parameters such as, but not limited to BMI, sex and medical conditions.

As used herein the term "about refers to 60 %. Alternatively the term about refers to ± 59 %, alternatively the term about refers to ± 58 %, alternatively the term about refers to ± 57 %, alternatively the term about refers to ± 56 %, alternatively the term about refers to ± 55 %, alternatively the term about refers to ± 54 %, alternatively the term about refers to ± 53 %, alternatively the term about refers to ± 52 %, alternatively the term about refers to ± 51 %, alternatively the term about refers to ± 50 %, alternatively the term about refers to ± 49 %, alternatively the term about refers to ± 48 %, alternatively the term about refers to ± 47 %, alternatively the term about refers to ± 46 %, alternatively the term about refers to ± 45 %, alternatively the term about refers to ± 44 %, alternatively the term about refers to ± 43 %, alternatively the term about refers to ± 42 %, alternatively the term about refers to ± 41 %, alternatively the term about refers to ± 40 %, alternatively the term about refers to ± 39 %, alternatively the term about refers to ± 38 %, alternatively the term about refers to ± 37 %, alternatively the term about refers to ± 36 %, alternatively the term about refers to ± 35 %, alternatively the term about refers to ± 34 %, alternatively the term about refers to ± 33 %, alternatively the term about refers to ± 32 %, alternatively the term about refers to ± 31 %, alternatively the term about refers to ± 30 %, alternatively the term about refers to ± 29 %, alternatively the term about refers to ± 28 %, alternatively the term about refers to ± 27 %, alternatively the term about refers to ± 26 %, alternatively the term about refers to ± 25 %, alternatively the term about refers to ± 24 %, alternatively the term about refers to ± 23 %, alternatively the term about refers to ± 22 %, alternatively the term about refers to ± 21 %, alternatively the term about refers to ± 20 %, alternatively the term about refers to ±

19 %, alternatively the term about refers to ± 18 %, alternatively the term about refers to ± 17 %, alternatively the term about refers to ± 16 %, alternatively the term about refers to ± 15 %, alternatively the term about refers to ± 14 %, alternatively the term about refers to ± 13 %, alternatively the term about refers to ± 12 %, alternatively the term about refers to ± 11 %, alternatively the term about refers to ± 10 %, alternatively the term about refers to ± 9 %, alternatively the term about refers to ± 8 %, alternatively the term about refers to ± 7 %, alternatively the term about refers to ± 6 %, alternatively the term about refers to ± 5 %, alternatively the term about refers to ± 4 %, alternatively the term about refers to ± 3 %, alternatively the term about refers to ± 2 % and alternatively the term about refers to ± 1 %.

Unless a numeral is already preceded by the term "about", each numeral recited herein and describing a dose or a time period referred to in the protocols of the present invention (e.g., the numerals describing the doses or the time periods referred to in Tables 1-83 and in the Claims section and the dose and time ranges described below) should be read as if the term "about" precedes it.

The term "immediately" as used herein refers to an immediate time. For example if step "x" immediately follows step "y", this may be understood to mean that there is no enforced waiting period between the two steps. It may be that a time interval passes between step "x" and "y" due to, for example, patient or apparatus preparation. Preferably, the time interval is less than 5 minutes, more preferably less than 3 minutes and even more preferably less than 1minute.

As used herein the term "simultaneously" refers to two events occurring at the same time with no enforced waiting period occurring between the two.

The term "radioimaging" as used herein refers to the imaging of the spatial distribution of a radiopharmaceutical which accumulates in a particular cell or sub-cellular component or cellular fluid.

The term "radiopharmaceutical" refers to a radioactive compound used for therapeutic, imaging, or diagnostic purposes in a mammalian subject.

The phrase "PET radiopharmaceutical" refers to any radiopharmaceutical that may be imaged using PET. An example of a PET radiopharmaceutical is 2-[F-18]fluoro-2-deoxy-D-glucose (FDG).

The phrase "myocardial perfusion" as used herein, refers to a normal or abnormal heart blood flow either at rest and/or following stress.

As used herein the phrase "lung perfusion" refers to a normal or abnormal lung blood flow.

The phrase "inflammatory process" as used herein, refers to the migration or infiltration of leukocytes into a pathological tissue. The process is typically driven by cytokines and/or chemokines as well as intracellular messengers) and involving vascular permeability, active migration of blood cells and passage of plasma constituents, resulting in tissue damage. The inflammatory process may be associated with any chronic or acute inflammation associated disease including, but not limited to inflammatory diseases associated with hypersensitivity, autoimmune diseases, infectious diseases, Graft rejection diseases, allergic diseases and cancerous diseases. Examples of diseases related to a bone inflammatory process include, but are not limited to muscular dystrophy, structural myopathy, inflammatory myopathy, a myotonic disorder, channelopathy, a metabolic muscle disease and arthritic disorders such as osteoporosis and osteoarthritis

The phrase "bone cancer" as used herein, refers to benign or malignant growth situated in the bone. The bone cancer may be a primary or secondary tumor.

As used herein, the phrase "breast cancer" refers to any type of malignant growth in the breast tissue.

The phrase "brain perfusion" as used herein, refers to a normal or abnormal blood flow to the brain. Typically, blood perfusion is imaged for the diagnosis of brain pathologies including but not limited to ischemia, stroke and dementia.

The phrase "tumor perfusion" as used herein refers to a blood flow to a tumor. Typically, tumor perfusion is imaged to identify a tumor and/or to monitor treatment, treatment response and multi-drug resistance.

As used herein, the phrase "liver structure" refers to any normal or abnormal structure in the liver including but not limited to a hemangioma, an abscess and overall liver enlargement.

Herein, the phrase "renal function" refers to any normal or abnormal function of the kidney including but not limited to filtration, tubular secretion, perfusion and secretion.

The phrase "liver function" refers to any normal or abnormal function of the liver, including but not limited to production of bile, production of blood plasma proteins, production of cholesterol, conversion of excess glucose into glycogen, regulation of blood levels of amino acids, processing of hemoglobin, conversion of ammonia to urea, clearing the blood of drugs and other poisonous substances, regulating blood clotting, producing immune factors and removing bacteria from the blood stream.

The phrase "cardiac vulnerable plaque", as used herein, refers to a deposit of fat, cholesterol and/or other materials that collect in arteries rendering same vulnerable to rupture.

As used herein, "prostate cancer" is defined as cancer of the prostate gland, typically adenocarcinoma of the prostate gland.

As used herein, the phrase "neuroendocrine tumor" refers to any tumor derived from cells that release a hormone in response to a signal from the nervous system. Examples of neuroendocrine tumors include, but are not limited to carcinoid tumors, islet cell tumors, medullary thyroid carcinoma, and pheochromocytoma. These tumors typically secrete hormones in excess, causing a variety of symptoms.

The term "thrombi" as used herein refers to blood clots that have not been released into the blood system.

As used herein, the phrase "parathyroid adenoma" refers to benign tumors of the parathyroid glands.

As used herein, the phrase "endocrine tumor" refers to a tumor derived from cells that release a hormone.

The phrase "pathological condition" as used herein, refers to a medical condition (e.g., a disease or a syndrome) including but not limited to cardiac pathological conditions, cancer and infection.

The phrase "myocardial ischemia" as used herein, refers to a state of inadequate blood supply to the heart, associated with impairment in the relaxation and contraction of the myocardium.

The term "schizophrenia" as used herein refers to a psychiatric disorder that includes at least two of the following: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms. Patients can be

diagnosed as schizophrenic using the DSM-IV criteria (APA, 1994, Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition), Washington, D.C.).

The term "Parkinson's disease" as used herein refers to a neurodegenerative disease associated with the destruction of brain cells that produce dopamine.

As used herein, the phrase "bone marrow activation" refers to an up-regulation of any of the functions of the bone marrow.

The term "osteomyelitis" refers to any inflammation of the bone marrow and adjacent bone.

Single photon emission computerized tomography (SPECT) and positron emission tomography (PET) are well known nuclear imaging systems in medicine. Generally, in nuclear imaging, a radioactive isotope is injected to, inhaled by or ingested by a patient. The isotope, provided as a radioactive-labeled pharmaceutical (radio-pharmaceutical) is selected based on bio-kinetic properties that cause preferential uptake by different tissues. The gamma photons emitted by the radio-pharmaceutical are detected by radiation detectors outside the body, giving its spatial and uptake distribution within the body, with little trauma to the patient.

SPECT imaging is based on the detection of individual gamma rays emitted from the body, while PET imaging is based on the detection of gamma-ray pairs that are emitted in coincidence, in opposite directions, due to electron-positron annihilations. In both cases, data from the emitted photons is used to produce spatial images of the "place of birth" of a detected photon and a measure of its energy.

Because PET imaging collects emission events, in the imaginary tubular section enclosed by the PET detectors, while SPECT imaging is limited to the solid collection angles defined by the collimators, generally, PET imaging has a higher sensitivity and spatial resolution than does SPECT. In PET, photon detectors also provide an indication of the time when a photon is detected.

It is possible to design SPECT imaging cameras with the sensitivity and resolution of PET imaging cameras. Furthermore, SPECT cameras comprising high spectral resolution are also available enabling their use in dual and multiple isotope studies. Voxel dynamic modeling allows the use of SPECT cameras for dynamic studies. For example, U.S. Pat. Appl. No. PCT IL2006/000059 assigned to Spectrum Dynamics LLC discloses the capabilities of a highly sensitive radioactive-emission SPECT camera, a result of a meticulous search for the many different effects that

combine synergistically to increase sensitivity and spatial, spectral, and time resolutions.

Inclusion of additional properties to the traditional SPECT imaging cameras requires the design of novel protocols which may be used for nuclear imaging. Such protocols may be used for diagnosing a myriad of diseases providing a higher degree of accuracy than presently used radioimaging protocols.

Thus, according to one aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 10-15 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected about 2 minutes following step (c);

(4) step (f) is effected about 30-60 minutes following step (d); and

(5) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is affected as described in Table 1.

According to another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (f) is effected about 30-60 minutes following step (e); and

(5) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is affected as described in Table 2.

According to yet another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 2 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is effected immediately following step (e);

(6) step (f) is for about 2 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 3.

According to still another aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is immediately following step (a);

(2) step (b) is for about 2 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 2 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 4.

According to an additional aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tl201 thallous chloride;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 20-30 mCi Tc99m sestamibi; and

(f) radioimaging the heart of the subject immediately following the peak stress, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15 minutes;

(2) step (c) is for about 2 minutes;

(3) step (e) is effected about 30 - 60 minutes following step (d); and

(4) step (f) is for about 2 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 5.

According to yet an additional aspect of the present invention there is provided method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 20-30 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a physical stress;

(e) administering to the subject at a peak of the physical stress about 3 mCi Tl201 thallous chloride;

(f) radioimaging the heart of the subject; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15-30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (f) is effected about 10-15 minutes following step (e);

(5) step (f) is for about 4 minutes;

(6) step (g) is effected about 4 hours following step (f); and

(7) step (g) is for about 6 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 6.

According to still an additional aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(f) radioimaging the heart of the subject; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 15-30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is effected immediately following step (e);

(6) step (f) is for about 4 minutes;

(7) step (g) is effected about 4 hours following step (f);

(8) step (g) is for about 6 minutes; and

(9) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 7.

According to a further aspect of the present invention there is provided method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(e) radioimaging the heart of the subject; and

(f) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a);

(2) step (b) is for about 2 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 4 minutes;

(7) step (f) is effected about 4 hours following step (e);

(8) step (f) is for about 6 minutes;

(9) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 8.

According to yet a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) allowing the subject to rest;

(c) radioimaging a heart of the subject;

(d) subjecting the subject to a pharmacological stress;

(e) administering to the subject at a peak of the pharmacological stress about 3 mCi Tl201 thallous chloride;

(f) allowing the subject to rest; and

(g) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 30 minutes;

(2) step (c) is for about 2 minutes;

(3) step (d) is effected immediately following step (c);

(4) step (e) is effected about 2 minutes following step (d);

(5) step (f) is for about 2 minutes;

(6) step (g) is effected immediately following step (f);

(7) step (g) is for about four minutes; and

(8) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 9.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 8-10 mCi Tc99m Teboroxime;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 20-30 mCi Tc99m Teboroxime; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following or during step (a);

(2) step (b) is for about 2-10 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following or during step (d);

(6) step (e) is for about 2-10 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 10.

According to still a further aspect of the present invention there is provided a method of radioimaging a lung perfusion, the method comprising simultaneously:

(a) administering to a subject less than about 5 mCi Tc99m Diethylene triamine-pentacetic acid (DTPA);

(b) administering to a subject less than about 5 mCi Tc99m MAA;

(c) radioimaging a lung of the subject, thereby radioimaging a lung perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) the Tc99m Diethylene triamine-pentacetic acid (DTPA) is administered via a nebulizer;

(2) step (c) is for about 0-30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 11.

According to still a further aspect of the present invention there is provided a method of radioimaging a bone inflammation or a bone cancer, the method comprising simultaneously:

(a) administering to a subject about 20-30 mCi Tc99m MDP; and

(b) radioimaging a bone of the subject, thereby radioimaging a bone inflammation or a bone cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 0-60 minutes following step (a);

(2) step (b) is for about six minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 12.

According to still a further aspect of the present invention there is provided a method of radioimaging an inflammatory process, the method comprising in sequence:

(a) administering to a subject about 2-3 mCi In 111 WBC; and

(b) radioimaging the subject, thereby radioimaging an inflammatory process.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a).

(2) step (b) is for about 1 minute.

According to still further features in the described preferred embodiments the method is effected as described in Table 13.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical stress;

(d) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10-15 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is immediately following step (b);

(4) step (e) is effected about 30-60 minutes following step (d); and

(5) step (e) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 14.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tc99m sestamibi;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical stress;

(d) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 15-30 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (e) is effected about 30-60 minutes following step (d); and

(5) step (e) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 15.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) subjecting the subject to a physical stress;

(c) administering to the subject at a peak of the physical stress about 3 mCi Tc99m sestamibi; and

(d) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a);

(2) step (d) is effected about 30-60 minutes following step (c); and

(3) step (d) is for about 5-15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 16.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject at a peak of the pharmacological stress about 3 mCi Tc99m sestamibi; and

(e) radioimaging the heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 minutes following step (a);

(2) step (b) is for about 15 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 15 minutes; and

(7) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 17.

According to still a further aspect of the present invention there is provided a method of radioimaging a breast cancer, the method comprising in sequence:

(a) administering to a subject about 0.3 mCi Tc99m sestamibi; and

(b) radioimaging a breast of the subject, thereby radioimaging a breast cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 15-30 minutes following step (a);

(2) step (b) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is, effected as described in Table 18.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) simultaneously administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO), no more than about 3 mCi Tc99m ECD and no more than about 5 mCi I123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 19.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 20.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 3 mCi Tc99m ECD; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 21.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 22.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 23.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi Tc99m ECD; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 24.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and

(b) radioimaging a brain of the subject, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 25.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver structure, the method comprising simultaneously:

(a) administering to a subject about 0.5 mCi Tc99m mebrofenin; and

(b) radioimaging a liver of the subject, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 26.

According to still a further aspect of the present invention there is provided a method of radioimaging a lung perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi of Tc99m DTPA and no more than 0.5 mCi of MAA or DTPA ln 111; and

(b) radioimaging a lung of the subject, thereby radioimaging a lung perfusion.

According to further features in preferred embodiments of the invention described below, step (b) is for about 6 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 27.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (thallium rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 4 mCi of Tl thallous chloride, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, wherein step (a) is for about 2-20 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 28.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (thallium stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 4 mCi Tl201 thallous chloride; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 2-20 minutes; and

(3) the pharmacological stress adenosine or dipyridamole .

According to still further features in the described preferred embodiments the method is effected as described in Table 29.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (teboroxime rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m teboroxime, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 30.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (teboroxime stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 4 mCi Tc99m Teboroxime; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 2-20 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 31.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (sestamibi rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m sestamibi, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 32.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (sestamibi stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 20-30 mCi of Tc99m sestamibi; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 33.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (tetrofosmin rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m tetrofosmin, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 34.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (tetrofosmin stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 20-30 mCi of Tc99m tetrofosmin; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following or during step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole .

According to still further features in the described preferred embodiments the method is effected as described in Table 35.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (Q12 rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 30 mCi of Tc99m Q12, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 36.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (Q12 stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 30 mCi of Tc99m Q12; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 37.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (BMIPP-I-123 rest), the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 5 mCi of BMIPP I-123, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 15 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 38.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion (BMIPP I-123 stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 5 mCi of BMIPP I-123; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 15 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 39.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to the subject at a peak of the physical stress about 30 mCi of a radiopharmaceutical; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b);

(2) step (c) is for about 10 minutes; and

(3) the pharmacological stress is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 40.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising simultaneously:

(a) radioimaging a heart of a subject; and

(b) administering to the subject about 30 mCi of a PET radiopharmaceutical, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (c) is effected immediately following step (b); and

(2) step (c) is for about 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 41.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, the method comprising simultaneously:

(a) radioimaging a tumor of a subject; and

(b) administering to the subject about 30 mCi of Tc99m Teboroxime, 30 mCi of Tc99m sestamibi, 30 mCi of Tc99m tetrofosmin or 4 mCi of Tl-201, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 5 minutes.

According to still further features in preferred embodiments of the invention described below, the method is effected as described in Table 42.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, the method comprising simultaneously:

(a) radioimaging a tumor of a subject; and

(b) administering to the subject about 4 mCi of Tl201 thallous chloride and no more than about 30 mCi of Tc99m sestamibi, thereby radioimaging a tumor.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 43.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising simultaneously:

(a) radioimaging a kidney of a subject; and

(b) administering to the subject about 1 mCi of Tc99mDTPA and about 3-10 mCi of Tc99mMAG3, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, step (a) is 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 44.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising simultaneously:

(a) radioimaging a kidney of a subject; and

(b) administering to the subject about 1 mCi of Tc99m DTPA and about 1 mCi of HippuranI-123, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, step (a) is about 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 45.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) radioimaging a brain of a subject; and

(b) administering to the subject about 20 mCi of Tc99m ECD (neurolite) and about 20 mCi of HPMAO 99m labeled and about 5 mCi of Spectaminel123, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 46.

According to still a further aspect of the present invention there is provided a method of radioimaging a brain perfusion, the method comprising simultaneously:

(a) radioimaging a brain of a subject; and

(b) administering to the subject no more than about 20 mCi of teboroxime, thereby radioimaging a brain perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is no more than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 47.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver structure, the method comprising simultaneously:

(a) radioimaging a liver of the subject; and

(b) administering to the subject no more than about 5 mCi of Tc99m sulfur colloid, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (a) is no more than 10 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 48.

According to still a further aspect of the present invention there is provided a method of radioimaging a liver function, the method comprising simultaneously:

(a) radioimaging a liver of the subject; and

(b) administering to the subject no more than about 10 mCi of Tc99m disida, thereby radioimaging a liver structure.

According to further features in preferred embodiments of the invention described below, step (a) is effected every five minutes for up until 1 hour.

According to still further features in the described preferred embodiments the method further comprises administering an agent for gall bladder contraction 1 hour following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 49.

According to still a further aspect of the present invention there is provided a method of radioimaging a gastric emptying, the method comprising simultaneously:

(a) radioimaging a stomach of a subject; and

(b) administering to the subject about 3 MBq of Tc99m Sulfer colloid or labeled 'solid food or 0.5 MBq In-111 DTPA labeled liquid food, thereby radioimaging a gastric emptying.

According to further features in preferred embodiments of the invention described below, step (a) is for a time until the stomach is empty of the labeled food.

According to still further features in the described preferred embodiments the method is effected as described in Table 50.

According to still a further aspect of the present invention there is provided a method of radioimaging a cardiac vulnerable plaque, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Tc99m annexin and no more than about 5mCi Tc99m AccuTec; and

(b) radioimaging a blood vessel of the subject, thereby radioimaging a cardiac vulnerable plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 51.

According to still a further aspect of the present invention there is provided a method of radioimaging for prostate cancer, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Prostascint containing 111In capromab pendetide; and

(b) radioimaging a prostate of the subject, thereby radioimaging for prostate cancer.

According to further features in preferred embodiments of the invention described below, the method comprises comprising at least one or more of the following:

(1) step (b) is effected about 24 - 72 hours following step (a);

(2) step (b) is less than 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 52.

According to still a further aspect of the present invention there is provided a method of radioimaging for SST receptor expressing tumors, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Octreotide containing 111 In DTPA; and

(b) radioimaging a body of the subject, thereby radioimaging for SST receptor expressing tumors.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 53.

According to still a further aspect of the present invention there is provided a method of radioimaging for neuroendocrine tumors, the method comprising in sequence:

(a) administering to a subject no more than about 20 mCi Tc99m Neotec; and

(b) radioimaging a body of the subject, thereby radioimaging for neuroendocrine tumors.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is less than about 30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 54.

According to still a further aspect of the present invention there is provided a method of radioimaging for thrombii, the method comprising in sequence:

(a) administering to a subject no more than about 20 mCi Tc99m Acutec; and

(b) radioimaging blood vessels of the subject.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected from about 0-20 minutes following step (a);

(2) step (b) is less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 55.

According to still a further aspect of the present invention there is provided a method of radioimaging a pheochromocytoma and/or myocardial failure, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi I-123 iofetamine hydrochloride MIBG; and

(b) radioimaging an adrenal gland and/or heart of the subject, thereby radioimaging a pheochromocytoma and/or myocardial failure.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (b) is less than about 30 minutes;

According to still further features in the described preferred embodiments the method is effected as described in Table 56.

According to still a further aspect of the present invention there is provided a method of radioimaging a cardiac stress, the method comprising in sequence:

(a) administering to a subject about 4 mCi Tl201 thallous chloride;

(b) radioimaging a heart of the subject;

(c) subjecting the subject to a physical or pharmacological stress, wherein the pharmacological stress is at least one vasodilatory agent; and

(d) radioimaging a heart of the subject, thereby radioimaging a cardiac stress.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 2 minutes following step (a);

(2) step (b) is for about 2-5 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected no more than about 5 minutes following step (c);

(5) step (d) is for about 2-10 minutes; and

(6) the at least one vasodilatory agent is adenosine or dipyridamole.

According to still further features in the described preferred embodiments the method is effected as described in Table 57.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising in sequence:

(a) administering to a subject about 2-4 mCi DTPA and/or Tc99mMAG3;

(b) radioimaging a kidney of the subject;

(c) subjecting the subject to a physical and/or at least one pharmacological stress; and

(d) radioimaging a kidney of the subject.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is for about 10-30 minutes;

(2) step (c) is effected immediately following step (b);

(3) step (d) is for about 10-30 minutes

(4) the pharmacological stress is selected from the group consisting of captopril fuside, a vasodilatory agent and a diuretic agent.

According to still further features in the described preferred embodiments the method is effected as described in Table 58.

According to still a further aspect of the present invention there is provided a method of radioimaging to determine Bexaar dosimetry, the method comprising simultaneously:

(a) radioimaging a body of a subject; and

(b) administering to the subject about 5 MCi/35 mg of I123 iofetamine hydrochloride, thereby radioimaging to determine Bexaar dosimetry.

According to further features in preferred embodiments of the invention described below, step (a) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 59.

According to still a further aspect of the present invention there is provided a method of radioimaging a parathyroid adenoma, the method comprising in sequence:

(a) administering to a subject about 1 mCi thallium 201thallous chloride and about 15mCi Tc99m pertechnetate;

(b) radioimaging a parathyroid of the subject, thereby radioimaging a parathyroid adenoma.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10 minutes following step (a); and

(2) step (b) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 60.

According to still a further aspect of the present invention there is provided a method of radioimaging a parathyroid adenoma, the method comprising in sequence:

(a) administering to a subject about 15 mCi Tc99m sestamibi and about 100 μCi I123;

(b) radioimaging a parathyroid of the subject, thereby radioimaging a parathyroid adenoma.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 10 minutes following step (a); and

(2) step (b) is for about 5 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 61.

According to still a further aspect of the present invention there is provided a method of radioimaging a thyroid cancer, the method comprising in sequence:

(a) administering to a subject about 10 mCi Tc99m MDP and about 4 mCi I-131;

(b) radioimaging a thyroid of the subject, thereby radioimaging a thyroid cancer.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 62.

According to still a further aspect of the present invention there is provided a method of radioimaging an endocrine tumor, the method comprising in sequence:

(a) administering to a subject about 15 mCi Tc99m MDP and about 4 mCi ln111 octeotride;

(b) radioimaging a body of the subject, thereby radioimaging an endocrine tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 63.

According to still a further aspect of the present invention there is provided a method of radioimaging an endocrine tumor, the method comprising in sequence:

(a) administering to a subject about 4 mCi ln111 octeotride;

(b) administering to a subject about 15 mCi Tc99m MDP;

(c) radioimaging a body of the subject, thereby radioimaging an endocrine tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 3 days following step (a);

(2) step (c) is effected no more than about 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 64.

According to still a further aspect of the present invention there is provided a method of radioimaging a prostate tumor, the method comprising in sequence:

(a) administering to a subject about 3 mCi ln111 capromab pentitide;

(b) administering to a subject about 15 mCi Tc99m RBCs;

(c) radioimaging a pelvis/abdomen of the subject, thereby radioimaging a prostate tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than about 3 days following step (a);

(2) step (c) is effected no more than about 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 65.

According to still a further aspect of the present invention there is provided a method of radioimaging a bone infection, the method comprising in sequence:

(a) administering to a subject about 3 mCi In111 WBC;

(b) administering to a subject about 15 mCi Tc99m colloid;

(c) radioimaging a bone of the subject, thereby radioimaging a bone infection.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected no more than 3 days following step (a);

(2) step (c) is effected no more than 2 hours following step (b); and

(3) step (c) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 66.

According to still a further aspect of the present invention there is provided a method of radioimaging a neck or head cancer invasion of a bone or cartilage, the method comprising in sequence:

(a) administering to a subject about 2 mCi Tl201 thallous chloride and about 15 mCi Tc99m MDP;

(b) radioimaging a bone or cartilage of the subject, thereby radioimaging a neck or head cancer invasion of a bone or cartilage.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 hours following step (a); and

(2) step (b) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 67.

According to still a further aspect of the present invention there is provided a method of radioimaging a pathological condition, the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111WBCs;

(b) administering to the subject about 1 mCi Tl201 thallous chloride and about 10 mCi Tc99m sestamibi; and

(c) radioimaging a body of the subject, thereby radioimaging a pathological condition.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 2 days following step (a); and

(2) step (c) is for about 30 minutes.

(3) the pathological condition is selected from the group consisting of an infection, a tumor and a myocardial infection.

According to still further features in the described preferred embodiments the method is effected as described in Table 68.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial ischemia, the method comprising in sequence:

(a) administering to a subject about 2 mCi I123 BMIPP;

(b) administering to the subject about 1 mCi Tl201 thallous chloride and about 10 mCi of a Tc99m labeled chemical selected from the group consisting of sestamibi and teboroxime; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial ischemia.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 48 hours following step (a); and

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 69.

According to still a further aspect of the present invention there is provided a method of radioimaging a pathological condition or a fever of unknown origin, the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111WBC;

(b) administering to the subject about 15 mCi 99m Fanoselomab; and

(c) radioimaging a body of the subject, thereby radioimaging a pathological condition or a fever of unknown origin.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a); and

(2) step (c) is for about 30 minutes.

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 70.

According to still a further aspect of the present invention there is provided a method of radioimaging to indicate schizophrenia or Parkinson's disease, the method comprising in sequence:

(a) administering to a subject about 2 mCi I123 IBZM;

(b) administering to the subject about 15 mCi Tc99m HMPAO; and

(c) radioimaging a brain of the subject, thereby radioimaging to indicate schizophrenia or Parkinson's disease.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a); and

(2) step (c) is for about 30 minutes.

(3) step (c) is effected immediately following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 71.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor, a tumor perfusion and/or for differentiating a tumor from infection the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111 WBC;

(b) administering to the subject Tc99m sestamibi, Tc99m Arcitumo Mab and Tl201 thallous chloride; and

(c) radioimaging an organ and/or a body of the subject, thereby radioimaging a tumor.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected about 5 minutes following step (b);

(4) a dose of Tc99m sestamibi and Tc99m Arcitumo Mab is each about 10 mCi; and

(5) a dose of Tl201 thallous chloride is about 1 mCi.

According to still further features in the described preferred embodiments the method is effected as described in Table 72.

According to still a further aspect of the present invention there is provided a method of radioimaging a renal function, the method comprising in sequence:

(a) administering to a subject about 2 mCi Iln111 DTPA;

(b) administering to the subject about 15 mCi Tc99m MAG3; and

(c) radioimaging a kidney of the subject, thereby radioimaging a renal function.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected about 5 minutes following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 73.

According to still a further aspect of the present invention there is provided a method of radioimaging a tumor perfusion, the method comprising in sequence:

(a) administering to a subject about 1 mCi Tl thallous chloride;

(b) administering to the subject about 15 mCi Tc99m teboroxime or about 15 mCi Tc99m sestamibi; and

(c) radioimaging an organ of the subject, thereby radioimaging a tumor perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 74.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion and apoptosis in blood vessel plaque, the method comprising in sequence:

(a) administering to a subject about 1 mCi Tl thallous chloride;

(b) administering to the subject about 15 mCi Tc99m Annexin; and

(c) radioimaging a heart and blood vessels of the subject, thereby radioimaging a myocardial perfusion and apoptosis in blood vessel plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected less than about 1 hour following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 75.

According to still a further aspect of the present invention there is provided a method of radioimaging to differentiate between infection and bone marrow activation, the method comprising in sequence:

(a) administering to a subject about 2 mCi ln111WBC;

(b) administering to the subject about 15 mCi Tc99m sulfur colloid; and

(c) radioimaging a body of the subject, thereby radioimaging a tumor perfusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 76.

According to still a further aspect of the present invention there is provided a method of radioimaging an osteomyelitis, the method comprising in sequence:

(a) administering to a subject about 2 mCi In111WBC;

(b) administering to the subject about 15 mCi Tc99m MDP; and

(c) radioimaging a bone of the subject, thereby radioimaging an osteomyelitis.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected immediately following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 77.

According to still a further aspect of the present invention there is provided a method of radioimaging an inflammation, the method comprising in sequence:

(a) administering to a subject about 5 mCi Gallium 67;

(b) administering to the subject about 15 mCi In111WBCs; and

(c) radioimaging a body of the subject, thereby radioimaging an inflammation.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes; and

(3) step (c) is effected about 72 hours following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 78.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion and apoptosis in blood vessel plaque, the method comprising in sequence:

(a) administering to a subject about 2 mCi In111 annexin;

(b) administering to the subject about 15 mCi Tc99m teboroxime or about 2 mCi Tl201 thallous chloride; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion and apoptosis in blood vessel plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is for about 30 minutes;

(3) step (c) is effected no more than about 3 minutes following step (b);

According to still further features in the described preferred embodiments the method is effected as described in Table 79.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 2 mCi Tl201 thallous chloride;

(b) administering to the subject about 15 mCi Tc99m pyrophosphate; and

(c) radioimaging a heart of the subject, thereby radioimaging a myocardial infusion.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected simultaneously with step (a);

(2) step (c) is for about 30 minutes; and

(3) step (c) is effected about 1 hour following step (b).

According to still further features in the described preferred embodiments the method is effected as described in Table 80.

A method of radioimaging a myocardial perfusion, the method comprising simultaneously:

(a) radioimaging a heart of the subject; and

(b) administering to a subject about 15 mCi of Tc99m pyrophsophate and about 2 mCi of Tl 201 thallous chloride, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, step (a) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 81.

According to still a further aspect of the present invention there is provided a method of radioimaging a myocardial perfusion or cardiac vulnerable plaque, the method comprising simultaneously:

(a) administering to a subject about 5 mCi ln111 annexin;

(b) administering to the subject about 5 mCi Tc99m Accutec;

(c) subjecting the subject to a pharmacological stress;

(d) administering to the subject about 1 mCi Tl201 thallous chloride; and

(e) radioimaging a heart and blood vessels of the subject, thereby radioimaging a myocardial perfusion or cardiac vulnerable plaque.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected about 24 hours following step (a);

(2) step (c) is effected immediately following step (b);

(3) the pharmacological stress is adenosine or dipyridamole;

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is for about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 82.

According to still a further aspect of the present invention there is provided a method of radioimaging a glucose metabolism, the method comprising simultaneously:

(a) administering to a subject about 30-50 mCi FDG; and

(b) radioimaging a body of the subject, thereby radioimaging a glucose metabolism.

According to further features in preferred embodiments of the invention described below, the method comprises at least one or more of the following:

(1) step (b) is effected immediately following step (a); and

(2) step (b) is for less than about 30 minutes.

According to still further features in the described preferred embodiments the method is effected as described in Table 83.

According to another aspect of the present invention there is provided a diagnostic pharmaceutical kit comprising

(i) a packaged dose unit of a first diagnostic radiopharmaceutical:

(ii) a packaged dose unit of a second diagnostic radiopharmaceutical;

(iii) a packaged dose unit of saline; and

(iv) a packaged dose unit of a pharmacological stress agent.

According to further features in preferred embodiments of the invention described below, the pharmacological stress agent is selected from the group consisting of adenosine, dipyridamole or dobutamine.

According to still further features in the described preferred embodiments the method is effected as described in Table 91.

According to still further features in the described preferred embodiments the method is effected as described in Table 92.

According to further features in preferred embodiments of the invention described below, the packaged dose unit of the first diagnostic radiopharmaceutical is a low dose.

According to further features in preferred embodiments of the invention described below, the low dose is about 2.5 mrem or less per kg body weight.

According to further features in preferred embodiments of the invention described below, the packaged dose unit of the second diagnostic radiopharmaceutical is a high dose.

According to further features in preferred embodiments of the invention described below, the high dose is about 30 mrem or more per kg body weight.

According to further features in preferred embodiments of the invention described below, each of the packaged dose units are associated with a portable computer-communicatable data carrier, the data carrier containing imaging protocol information for use with the packaged dose units.

According to yet another aspect of the present invention, there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject a low dose of a first radiopharmaceutical;

(b) subjecting the subject to a physical stress;

(c) administering to the subject at a peak of the physical stress a medium or high dose of a second radiopharmaceutical;

(d) immediately radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, the first radiopharmaceutical and the second radiopharmaceutical are identical.

According to further features in preferred embodiments of the invention described below, the first radiopharmaceutical and the second radiopharmaceutical are not identical.

According to further features in preferred embodiments of the invention described below, a length of time of steps a-d is no more than 20 minutes.

According to further features in preferred embodiments of the invention described below, a length of time of steps a-d is no more than 30 minutes.

According to further features in preferred embodiments of the invention described below, the method comprises only one radioimaging step.

According to further features in preferred embodiments of the invention described below, the method further comprises radiomaging a heart of the subject following step (a).

According to another aspect of the present invention, there is provided a method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject a radiopharmaceutical;

(b) immediately radioimaging a heart of the subject, thereby radioimaging a myocardial perfusion.

According to further features in preferred embodiments of the invention described below, a length of time of steps a-b is no more than 10 minutes.

According to further features in preferred embodiments of the invention described below, the methods of the present invention further comprise administering to the subject a trace amount of radiopharmaceutical prior to step (a).

According to further features in preferred embodiments of the invention described below, the methods of the present invention further comprise radioimaging an organ of interest following the administering the trace amount of radiopharmaceutical.

The protocols of the present invention are further exemplified in the Examples section which follows.

The protocols of the present invention generally comprise administration of a radiopharmaceutical to a subject followed by imaging of a target organ. A waiting period may be added between the two steps to allow for distribution of the radioisotope in the body and clearance from organs such as the liver. According to various protocols of the present invention, the subject is also subjected to either a physical or pharmacological stress. In some case the subject may be subjected to both stresses (in sequence) in a single imaging protocol.

These individual steps may be further customized according to a patient's specific parameters. Thus, the dose of the radiopharmaceutical, waiting time/resting time, length of physical stress, degree of physical stress, dose of pharmacological stress and/or acquisition time may all be further fine-tuned and adjusted (customized) according to specific patient parameters. Examples of such parameters include, but are not limited to the patient's age, patient's sex, BMI, rate of metabolism, smoking, the nature of therapeutic treatments which the patient has undergone and the patient's medical condition (e.g. blood pressure, pregnancy, breast feeding, diabetes).

Thus, for some applications, one or more of the following parameters of the radiopharmaceutical agent are customized:

- the dose, or for multiple radiopharmaceutical agents, the respective doses;
- the radioactivity;
- for cocktails, the ratio of the different radiopharmaceutical agents; and/or
- the volume of the dose, or for multiple radiopharmaceutical agents, the volumes of the respective doses.

For some applications, one or more of the following parameters of the administration are customized:

- the dose administered, or for multiple radiopharmaceutical agents, the respective doses per administration;
- the type of administration, e.g., a single bolus, a plurality of boluses (e.g., two boluses), pulsatile administration, or constant drip administration;
- the labeled radiopharmaceutical agent for each administration, whether a single agent or a cocktail of agents;
- the time of the administration with respect to the time of imaging;

- the timings of multiple administrations with respect to each other and with respect to other activities, such as rest or stress (physical or pharmacological);
- the administration device, e.g., a syringe, a dual-needle syringe, a pump, or an IV line; and/or
- the mode of administration, e.g., manual, automatic, or computer driven.

Further details on customization are provided in Figures 99A-E.

As mentioned, all the protocols of the present invention comprise administration of at least one radiopharmaceutical.

Selection of a radiopharmaceutical for imaging a particular process/organ is dependant on its distribution in the body. For example ^{201}Tl Thallium Chloride mimics the biochemical and physiological distribution of potassium in the heart muscle and thus may be used to radioimage cardiac perfusion. The myocardial uptake of Tc99m sestamibi appears to occur by a passive diffusion process. The rate of passive uptake is determined by the membrane permeability of the radiopharmaceutical and the surface area of the vascular beds to which it is exposed; thus myocardial uptake is related to myocardial blood flow. While the mechanism of myocardial retention is not completely understood, it has been suggested that Tc99m sestamibi is trapped in the proximity of the mitochondria mostly due to its charge. Other radiopharmaceuticals suitable for cardiac imaging include but are not limited to Tc99m teboroxime and Tc99m tetrofosmine. When injected at rest, these radiopharmaceuticals accumulate in viable myocardial tissue; infarcts are thus delineated as areas of lack of accumulation. When injected at stress (either exercise or pharmacologic vasodilation), they accumulate in myocardial tissue in relation to myocardial blood flow; thus ischemic areas (e.g., those supplied by stenotic vessels) are detected as areas of less accumulation.

According to the protocols of the present invention, Tc99m sestamibi may also be used to image tumors such as parathyroid and thyroid tumors and breast cancer. Although the precise mechanism of tumor localization is unclear, it has been suggested that Tc99m sestamibi passively crosses cell membranes and is concentrated primarily within cytoplasm and mitochondria. It has been proposed that malignant cells, because of their increased metabolic rate, maintain greater negative mitochondrial and transmembrane potentials, thus enhancing intracellular

accumulation of Tc99m sestamibi. In thyroid glands with hyperthyroidism, blood flow and the number of mitochondria are increased, which may explain the uptake of Tc99m sestamibi in hyperthyroid glands. Localization of Tc99m sestamibi appears to be dependent on blood flow to the tissue, the concentration of Tc99m sestamibi presented to the tissue, and the size of the gland.

The radiopharmaceuticals used in the protocols of the present invention may be dispensed to the subject using any mode of administration. Suitable routes of administration may, for example, include oral, rectal, transmucosal, especially transnasal, intestinal or parenteral delivery, including intramuscular, subcutaneous and intramedullary injections as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Typically, the radiopharmaceuticals are administered parenterally. Thus, the radiopharmaceuticals described herein may be formulated for parenteral administration, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multidose containers with optionally, an added preservative. The compositions may be suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

According to some aspects of the present invention, two radiopharmaceuticals are administered simultaneously to a subject. Typically, the radiopharmaceuticals are administered one after the other, preferably in separate syringes and not administered as a co-formulation.

It will be appreciated that the dose of the radiopharmaceutical may be selected from a range of acceptable low, medium or high doses, as further described hereinbelow. Preferred doses of radiopharmaceuticals used in each protocol are provided in the Examples section which follows. It should be appreciated, though, that each of the protocols of the present invention may also be practiced using other doses which fall under their corresponding low, medium or high doses. The doses provided in Tables 1-83 of the Examples section hereinbelow have been grouped into low range, medium range and high range doses as detailed infra.

An exemplary range of a low dose of tagged Tc 99m is up to about 20 mCi or more specifically about 2-12 mCi e.g. about 3.

An exemplary range of a medium dose of tagged Tc 99m is between about 20-30 mCi or more specifically about 22-28 mCi e.g. about 25 mCi.

An exemplary range of a high dose of tagged Tc 99m is above 30 mCi or more specifically 30-40 mCi e.g. 35 +/- 25 %.

An exemplary range of a low dose of tagged Tl 201 is up to about 1 mCi or more specifically about 0.1-0.5 mCi e.g. about 0.3 mCi.

An exemplary range of a medium dose of tagged Tl 201 is between about 1 - 3 mCi or more specifically about 1.5 – 2.5 mCi e.g. about 2 mCi.

An exemplary range of a high dose of tagged Tl 201 is above about 3 mCi or more specifically about 3-5 mCi e.g. about 4 mCi.

An exemplary range of a low dose of tagged In 111 is up to about 2 mCi or more specifically about 0.5-1.5 mCi e.g. about 1 mCi.

An exemplary range of a medium dose of tagged In 111 medium dose is between about 2 - 3 mCi or more specifically about 2.2 – 2.8 mCi e.g. about 2.5 mCi.

An exemplary range of a high dose of tagged In 111 is above about 3 mCi or more specifically about 3-5 mCi e.g. about 4 mCi.

An exemplary range of a low dose of tagged I 123 is up to above 5 mCi or more specifically about 2 - 4 mCi e.g. about 3 mCi.

An exemplary range of a medium dose of tagged I 123 is between about 5 - 10 mCi or more specifically about 6 - 8 mCi e.g. about 7 mCi.

An exemplary range of a high dose of tagged I 123 is above about 10 mCi or more specifically about 10 - 15 mCi e.g. about 13 mCi.

An exemplary range of a low dose of tagged Gallium is up to about 5 mCi or more specifically about 2 - 4 mCi e.g. about 3 mCi.

An exemplary range of a medium dose of tagged Gallium is between about 5 - 10mCi or more specifically about 6.5-8.5 mCi e.g. about 7 mCi.

An exemplary range of a high dose of tagged Gallium is above about 10 mCi.

An exemplary range of a medium dose of free I 123 medium is between about 0.05 - 2 mCi or more specifically between about 0.1-0.5 mCi e.g. about 0.25 mCi.

An exemplary range of a high dose of free I 123 is above about 2 mCi or more specifically about 2-5mCi e.g. about 3 mCi.

The radiopharmaceuticals used in the protocols of the present invention are all commercially available. For example, thallous chloride tl201 is commercially

available from Mallinckrodt Inc, St. Louis, U.S.A. ^{18}fluorine-labeled-2-fluoro-2-deoxyglucose is commercially available from such Companies as Health Imaging Isotopes. Tc99m Sestamibi is commercially available as Cardiolite®, or Miraluma ® (Bristol Myers Squib – Medical Imaging) and Tc99m tetrofosmin is commercially available as Myoview, (Amersham Int.). I-123 BMIPP is a fatty acid imaging agent that has been available in Japan for many years, and is currently in Phase III clinical trials in the United States.

As mentioned above, the protocols of the present invention may comprise administration of a pharmacological agent. Typically, such pharmacological agents are administered by infusion I.V.

It will be appreciated that the protocols of the present invention may be preceded by administration of a trace amount of radiopharmaceutical (e.g. a tenth of a low dose of the radiopharmaceutical, or less, such as less than 2 mCi or less than 1 mCi) and the organ of interest may be prescanned to tune in and optimize the later phase of the scanning. Regardless of the radioisotope employed, concomitantly with of following radioisotope administration, radioimaging is effected. Since the imaging technique is performed in vivo, preferably nuclear imaging is utilized.

Generally, nuclear imaging is aimed at visualizing molecular and cellular processes occurring in living tissues. As such, nuclear imaging typically serves as a medical tool for measuring signals of molecules within the tissue and thus for generating quantitative images of physiological, biochemical and pharmacological function.

PET or SPECT imaging may be used to execute the protocols of the present invention. Preferably SPECT radioimaging is performed. SPECT imaging detects isotopes that decay by electron capture and/or gamma emissions. Certain proton-rich radioactive isotopes, such as ^{123}I and Tc99m are capable of capturing an orbiting electron, transforming a proton to a neutron [Sorenson J A, and Phelps M E. Philadelphia: W. B. Saunders; 1987]. The resulting daughter nucleus often remains residually excited. This meta-stable arrangement subsequently dissipates, thereby achieving a ground state and producing a single gamma photon in the process. Because gamma photons are emitted directly from the site of decay, no comparable theoretical limit on spatial resolution exists for SPECT. However, instead of coincidence detection, SPECT utilizes a technique known as collimation [Jaszczak R

J. Boca Raton: CRC Press; (1991): 93-118]. A collimator may be thought of as a lead block containing many tiny holes that is interposed between the subject and the radiation detector. Given knowledge of the orientation of a collimator's holes, the original path of a detected photon is linearly extrapolated and the image is reconstructed by computer-assisted tomography.

Position tracking devices per se are well known in the art and may use any one of a plurality of approaches for the determination of position in a three-dimensional space as is defined by a system of coordinates in three and up to six degrees-of-freedom. Some position tracking devices employ movable physical connections and appropriate movement monitoring devices to keep track of positional changes. Thus, such devices, once zeroed, keep track of position changes to thereby determine actual positions at all times.

Radioactive emission detectors are well known in the art and may use any one of a number of approaches for the determination of the amount of radioactive emission emanating from an object or portion thereof. Depending on the type of radiation, such detectors typically include substances which when interacting with radioactive decay emitted particles emit either electrons or photons in a level which is proportional over a wide linear range of operation to the level of radiation impinging thereon. The emission of electrons or photons is measurable and therefore serves to quantitatively determine radiation levels. Solid-state radioactive emission detectors include CdZnTe detectors, CdTe detectors, HgI detectors, Si detectors, Ge detectors. etc. Scintillation detectors include NaI(Tl) detectors, GSO detectors, CsI detectors, CaF detectors, etc. Also known are gas detectors and scintillation fiber detectors.

Thus, as now afforded by the present embodiments, connecting one or more radioactive emission detectors to the position tracking system permits simultaneous radioactivity detecting and position tracking at the same time. This enables the accurate calculation of the shape, size and contour of the radiating object and its precise position in a three-dimensional space.

Preferably, the SPECT cameras used in the protocols of the present invention have a high sensitivity and resolution.

Properties which may be combined to increase a traditional SPECT imaging camera's sensitivity and resolutions include:

1. solid collection angles greater than 0.1 or 0.15 steradians;

2. close proximity of the detectors to the body, in order to increase both:

i. detection efficiency, which falls as a proportionally to the square of the distance from an object; and

ii. resolution, where the number of detector pixels which view an object also falls proportionally to the square of the distance from the object;

3. windshield-wiper sweeping motions, with a center of rotation outside the patient's body, to maximize the information obtained from each x;y;z detector position;

4. trio-vision of each voxel, wherein each voxel is viewed with x, y, and z, components, as opposed to stereo vision in a plane, with only x and y components of state-of-the-art cameras;

5. Focus on a region of interest, by:

i. prescanning;

ii. independent motion of detectors, for independent focusing on ROI, by each detector;

iii. applying algorithm which select a preferred set of views to for ROI focusing, based on the geometry of the organ to be imaged;

iv. zooming in, by a second algorithm tic iteration, to select a preferred set of views based on earlier findings;

v. active vision, which ensures that each detector obtains the maximum information from any position;

6. calibration sources, which may be placed on the body, within a body lumen, or near the camera;

7. the use of the calibration sources of (6) to obtain an attenuation map;

8. ultrasound-based, or MRI based attenuation correction;

9. ultrasound-based attenuation correction using ultrasound patches, such as patch-sensor devices, described in U.S. Patents 5,807,268; 5,913,829 and 5,885,222, all of which are assigned to MedAcoustics, Inc., Raleigh, NC, USA, both for structural mapping, for correlating the structural map with the functional map, and for attenuation correction. The ultrasound patches may be incorporated with the radiopharmaceutical calibration sources; and

10. minimal multiplexing between the detectors and the analyzer, to prevent saturation;

The camera may comprise a plurality of detectors, each of which is coupled to a respective angular orientator. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. For example, the array may include 16x64 pixels. A control unit drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). The control unit produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

The camera may be configured to begin an image acquisition procedure by performing a relatively brief, preliminary scan, and, based on the results of this preliminary scan, to determine one or more parameters of the full image acquisition procedure, such as dwell time per orientation of each detector. Typically, this determination further takes into account imaging protocol and/or patient-specific information received by imaging system from patient-specific data carrier, such as the activity of the labeled radiopharmaceutical agent at the time of administration, the time of administration, the patient's BMI (which may be used to estimate a perfusion percentage), and the pharmacokinetics of the labeled radiopharmaceutical agent.

In another embodiment, the camera may be configured to individually set a total angular range of each of the detectors responsively to the detector's orientation with respect to the ROI. For example, at least one detector closer to the ROI (a "proximal detector" or an "inner detector") may have a greater total angular range than at least one detector further from the ROI (a "distal detector" or an "outer detector"). The distal detectors are typically located nearer to the ends of a frame holding the detectors, while the proximal detectors are typically located nearer to center of the frame. The use of narrower angular ranges for some of the detectors generally reduces the photon acquisition time spent by these detectors in orientations aimed outside of the ROI. Alternatively, at least one distal detector has a greater total angular range than at least one proximal detector. In order to reduce the total angular range for a given detector, the camera typically drives the associated angular orientator to: (a) increase the dwell time of the detector in at least a portion of its orientations, and/or (b) reduce the angle by which the detector is moved during each orienting of the detector. For some applications, the camera sets the angular range of the detectors based on protocol information received by imaging system from patient-

specific data carrier. For example, the number of distal and proximal detectors, and their respective angular ranges, may be specified by the protocol information.

The camera may also comprise a plurality of detectors, each of which is coupled to a respective angular orientator. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. The control unit drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). The control unit produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

In another embodiment, the camera is configured to drive one of the orientators to move its respective detector through a plurality of sequential angular positions, e.g., positions 1, 2, 3, ..., 18, 19, and 20. Typically, a linear relationship relates the sequential positions, such that, for example, positions 1, 2, 3, ..., 20 represent 1°, 2°, 3°, ..., 20°, or, 2°, 4°, 6°, ..., 40°. Alternatively, a non-linear relationship relates the sequential positions. Higher or lower angular resolutions are typically obtainable, as well.

For some applications, the camera steps the orientator in a first pass through a subset of the positions spanning most of the range of positions, and in a second pass the camera steps the orientator through a different subset of the positions. At each position, data are acquired by the detector. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17, and the detector acquires data at each of these positions. During the second pass, the orientator steps through positions 2, 6, 10, 14, and 18. During two subsequent passes, data are acquired at the remainder of the positions. In this manner, a single-direction interlaced scan of the data is acquired by camera 452.

In an embodiment, a back-and-forth interlaced scan is acquired in which data are sampled when the orientator is moving in both directions. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17. During the second pass, the orientator steps through positions 18, 14, 10, 6, and 2. During the third pass, the orientator steps through positions 3, 7, 11, 15, and 19, while during the fourth pass, the orientator steps through positions 20, 16, 12, 8, and 4. Fifth and higher passes, if desired, typically repeat the motions used in the earlier passes.

For some applications, the positions in a pass are not ordered from lowest-to-highest or highest-to-lowest. For example the positions of a pass may be 1, 15, 11, 19, and 17. Typically, the positions are, however, distributed generally evenly throughout the range of positions, in order to acquire photon counts representative of the entire region of interest.

As appropriate for a given scanning protocol using interlaced scanning, one or more, or even all of the orientators are driven to step through their respective positions in an interlaced fashion.

Typically, execution of an interlaced scan as provided by these embodiments of the present invention allows an operator of the camera, such as an imaging technician or other healthcare worker, to acquire a high-resolution image of the ROI in about 105 % to 115 % of the amount of time as would be used if orientator 456 were stepped through the positions sequentially. (Typically, each orientation takes between about 50 and about 200 msec, depending upon the angle of the step.) The high-resolution image is completely acquired after the orientator has stepped through each of its positions. In some cases, additional value is attained by interlacing the scanning, however, as this allows the performance of dynamic studies, in which a plurality of images are acquired during a respective plurality of the time periods, i.e., during each complete pass of the orientator. Although each these images is typically of lower resolution than the high-resolution image acquired using photon counts acquired during all of the passes, the images nevertheless have sufficient resolution to produce clinically-meaningful data for each time period of a dynamic study.

For some applications, interlacing the scanning allows an operator to see an initial, lower-resolution scan of the ROI. If, for example, an adjustment of any form is desired, this can often be seen within the first few seconds of a scan. The present scan is terminated, the adjustment made, and a second scan initiated. In the absence of interlacing, it is typically necessary to wait until a scan has completed until an assessment of the scan's results can be made.

For some applications, it is desirable to know whether the patient has moved during a scan. Patient movement is one reason for lower quality images, and when identified it can typically be corrected by suitable instruction and then a second scanning procedure initiated. Interlaced scanning, as provided by these embodiments of the present invention, allows the operator to immediately assess whether there has

been patient movement between one pass and a subsequent pass. In an embodiment, the imaging system displays to an operator the scans obtained from the various passes in rapid succession at the same location on a monitor. As appropriate, the imaging system cycles quickly through the scans repeatedly (e.g., pass 1, pass 2, pass 3, pass 4, pass 1, pass 2, pass 3, pass 4...), e.g., displaying each scan for between about 0.2 and about 2 seconds, allowing an operator to see whether there is jitter between successive scans. If so, patient movement is typically the cause and image acquisition is repeated. For some applications, the scan is acquired in exactly two passes, e.g., the orientator steps through positions 1, 3, 5, ..., 19 during a first pass, and through positions 2, 4, 6, ..., 20 during a second pass, or through positions 20, 18, 16, ..., 2 during the second pass.

Images acquired using these techniques, or other non-interlacing techniques described herein, are generally used to perform one or more of the following image reconstructions: (a) reconstruction of intensity image, (b) reconstruction of intensity over time, followed by fitting a model of the kinetics (which describe for each voxel a parameter set describing its time curve), and followed by presenting a three-dimensional map of the parameters, and/or (c) direct reconstruction of a three-dimensional parametric representation, without performing a reconstruction of an intensity map, typically by plugging an equation of a kinetic model into a reconstruction algorithm, and generating a result directly in terms of the value of the parameters per voxel (the parameters may include, for example, flow, diffusion coefficients, metabolism rate, or bio-clearance rate).

The camera sensitivity may be determined by at least one of the following:

1. a sensitivity in terms of speed of data collection and spatial resolution, at least as good as a gold standard for PET imaging for at rest myocardial perfusion with N-13-ammonia (NH_3);

2. a sensitivity sufficient for reconstructing an image under a Cobalt wire Nema test of a line source of 5 mCi cobalt with a line spread function of less than 7 mm Full Width Half Maximum (FWHM) through air at a distance of at least 100 mm;

3. a sensitivity sufficient for resolving through air at a distance of at least 100 mm under a Nema Bar Phantom test of gaps formed between 1 mm wide led bars positioned less than 7 mm apart from one another over a uniform cobalt disc;

4. a sensitivity operative for image acquisition of a full organ in less than 10 seconds at a spatial resolution, capable of identifying objects not greater than about 7 mm X 7 mm X 7 mm with a signal-to-noise ratio of at least 4 to 1 or better;

5. a sensitivity for detecting at least 1 out of every 5000 emitted photons while allowing a reconstructions of a 3D image with a resolution of not more than 5 mm and energy resolution of not more than 15 %; and

6. having a sensitivity to image a volume of about 5cm diameter located about 150 mm from the detectors, with a total sensitivity of about 1 photons detected out of 65 emitted.

According to some embodiments of the aspects of the present invention, the SPECT imaging apparatus comprises voxel kinetic compartmental modeling allowing its use for dynamic studies i.e. a quantitative measurement of flow. Alternatively, or additionally, a two step imaging for dynamic studies may be performed, based on small anatomic region of interest. For example, as a first step, conventional injection and imaging is performed, using standard voxel division, for example, of 5 X 5 X 5 mm, to obtain an image of the target, for example, the heart.

An anatomical region of interest is then defined on the image, and a new voxel map is generated, along the anatomical boundary lines. The anatomical region of interest may be a small portion of the overall image.

As a second step, a second injection is made, followed by scanning with detecting recourses aimed at the anatomical region of interest.

In a way, this approach is suggestive of a zooming in approach, for example, as taught in commonly owned PCT/IL2005/001173. But there, voxel reconstruction was rigorous throughout, and here, the first step employs cubical voxels, as known, but these are used to define anatomical voxels for the second step.

Several radioimaging protocols may be employed for this purpose, for example, as follows:

Step 1: a first injection, for example, a single bolus of a first marker, such as Tl-201, at a low dose of between 0.5 and 2 mCi, and imaging the heart for example, for about 1 minutes, to acquire a high quality image, to be used for constructing the anatomical image, and for defining a finer region of interest; and

Step 2: while the patient is immobile, injecting 20-40 mCi, preferably of a second marker, for example, Tc-99m-sestamibi, and performing an up to 10 minute

dynamic study, with image reconstruction every several seconds, for example, every 5 or 10 or 20 seconds, the dynamic image being superimposed on the first image.

On the one hand, when the image reconstruction is anatomically defined, the number of variables decrease drastically, for example, by a factor of 10;

Additionally, where only a small anatomically defined region is of interest, the scanning sweep is considerably shortened.

Both these factors together reduce the scanning time necessary for obtaining informative images for the anatomically defined region of interest.

In consequence, the two step rigorous-to-anatomic protocol is a highly effective technique for dynamic studies, providing anatomically reconstructed data, at very short time intervals of several seconds, and enabling the acquisition of kinetic parameters of specific tissues and across different tissues.

It will be appreciated that other markers may be used, and for other durations, provided the basic scheme of a first image for defining the anatomical boundaries, and the second image for dynamic reconstruction of anatomical voxels is maintained.

According to a particular embodiment the imaging apparatus is a high-definition SPECT camera, for example, which during imaging, is capable of acquiring at least one of 5000 photons emitted from the region of interest during the image acquisition procedure, such as at least one of 4000, 3000, 2500, 2000, 1500, 1200, 1000, 800, 600, 400, 200, 100, or 50 photons emitted from the region of interest. In one particular embodiment, the camera is capable of acquiring at least one of 2000 photons emitted from the ROI during the image acquisition procedure.

According to another embodiment, the imaging apparatus is a high-definition SPECT camera, for example, which during imaging, is capable of acquiring at least 200,000 photons, such as at least 500,000, 1,000,000, 2,000,000, 3,000,000, 4,000,000, 5,000,000, 8,000,000, or 10,000,000 photons, emitted from a portion of the ROI having a volume of no more than 500 cc, such as a volume of no more than 500 cc, 400 cc, 300 cc, 200 cc, 150 cc, 100cc, or 50 cc. In one particular embodiment, the camera is capable of acquiring at least 1,000,000 photons emitted from a volume of the region of interest having a volume of no more than 200 cc

A particularly preferred imaging apparatus which may be used during the protocols of the present invention is that taught in PCT IL2006/000059 assigned to Spectrum Dynamics LLC.

Whichever camera is selected for use, the imaging parameters may be specifically tailored to an individual subject. For instance, individual detector integration time may be set according to the patient BMI, injected dose and time of injection. According to one embodiment of this aspect of the present invention, patients are categorized into 3 or more different groups based on BMI and individual detector integration times are set accordingly. Detector span may also be individually customized according to the physical characteristics of the patient (e.g. chest width) and the size of the region of interest specified in the protocol.

Thus, for some applications, one or more of the following parameters of the imaging procedure are customized. For some applications, such parameters are separately specified for individual components of the camera of the imaging system or groups of components.

- total acquisition time, and/or acquisition time for a plurality of phases of acquisition;
- detector scanning plan, including detector motions, such as detector angular and translational motions, detector step size (i.e., the density of the step size, typically expressed in degrees), number of detectors utilized for image acquisition, and detector dwell time at each view;
- detector sensitivity;
- detection energy resolution;
- detector calibration plan;
- definition of the region of interest (ROI);
- gating parameters;
- energy bands, i.e., a plurality of non-overlapping energy windows;
- collimator positioning, shape, structure, and orientation;
- multiple/interlaced scans;
- zooming parameters;
- uniformity/non-uniformity of scan;
- Compton scatter map calculation and correction parameters;
- optimal energy window;
- optimal energy resolution, i.e., the range of energy level windows for which detection is enabled; and/or

- adaptivity of scan pattern to acquired counts, e.g., active vision parameters (as described in the above-mentioned International Application PCT/IL2005/001173).

Similarly, in some embodiments, the protocols are performed with a range of acquisition durations (total scan times). It will be appreciated that the duration of the acquisition time (or any other time mentioned in the protocols e.g., resting, waiting) may be selected from a range of acceptable short, medium or long durations, as further described hereinbelow. Preferred acquisition time durations used in each protocol are provided in the Examples section which follows. It should be appreciated, though, that each of the protocols of the present invention may also be practiced using other acquisition durations which fall under their corresponding short, medium or long times as further exemplified for a single organ in Table 84 of the Examples section hereinbelow and for a whole body/ multisegment scan in Table 85 of the Examples section hereinbelow. A typical duration of a dymamic study may last from about 5 sec-30 min, about 10 sec-20 min, about 20 sec-10 min, about 30 sec-7min, about 60 sec-360 sec, about 90 sec-240 sec, for example about 120 sec.

Other protocol values, such as waiting times, energy windows/resolution, angular range, angular step, and dwell time, may also have a range from 50 %, 75 %, 90 %, or 100 % of the value given for the respective protocol, up to 5 times the value given for the respective protocols.

The protocols of the present invention may be selected according to a patient's indications, physical status and medical condition. The cardiac imaging protocols of the present invention may comprise a single imaging stage or two imaging stages. Such cardiac imaging protocols typically differentiate between healthy cardiac tissue and scarred or poorly perfused cardiac tissue. Perfusion defects that appear after exercise or pharmacologic stress suggest either vascular occlusion or myocardial infarction. For some applications, such studies are performed gated to the patient's ECG, in order to study cardiac wall motion. Wall motion studies allow calculation of key cardiac function parameters, such as ejection fraction and estimated cardiac output.

In respective embodiments of the present invention, all of the protocols described herein and/or in the co-assigned patent applications incorporated herein by reference are enabled to generate clinically-valuable images. A "clinically-valuable

image" is an image of an intra-body region of interest (ROI) containing the labeled radiopharmaceutical agent(s), which image may be used for diagnosing a disease and/or evaluating a treatment regimen.

The image may have a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, in at least 50% of the reconstructed volume, wherein the labeled radiopharmaceutical agent as distributed within the ROI has a range of emission-intensities R (which is measured as emitted photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional emission-intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25 %, 20 %, 15 %, 10 %, 5 %, 2 %, 1 %, or 0.5 % of range R. For example, the agent may emit over a range from 0 photons/second/cc to 10^5 photons/second/cc, such that the range R is 10^5 photons/second/cc, and at least 50 % of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 15 % of range R, i.e., less than 1.5 x 10^4 photons/second/cc. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50% of the voxel have inaccuracies of less than 15% of range R;

The image may be generated according to a protocol, including at the radiopharmaceutical dose and image acquisition duration specified by the protocol, the image has a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein the labeled radiopharmaceutical agent has a range of intensities R (photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25 %, 20 %, 15 %, 10 %, 5 %, 2 %, 1 %, or 0.5 % of range R. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel; and/or

The image may also have a resolution of at least 20x20x20 mm, such as at least 15x15x15 mm, 10x10x10 mm, 7x7x7 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein values of parameters of a physiological process modeled by a parametric representation have a range of physiological parameter values R, and wherein at least 50% of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 100% of range R, such as less than 70 %, 50 %, 40

%, 30 %, 25 %, 20 %, 15 %, 10 %, 5 %, 2 %, 1 %, or 0.5 % of range R. For example, the physiological process may include blood flow, the values of the parameters of the physiological process may have a range from 0 to 100 cc / minute, such that the range R is 100 cc / minute, and at least 50 % of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 25 % of range R, i.e., less than 25 cc / minute. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50 % of the voxels have inaccuracies of less than 25 % of range R.

The information gleaned from the protocols of the present invention may be used for diagnosis of a disease or disorder. Accordingly, using the imaging data obtained from the protocols of the present invention, together with other criteria such as age, obesity, cholesterol level, HDL and LDL levels, smoking, and the like which are well known to those skilled in the art, a skilled artisan will be able to predict the likelihood that the subject will develop a vascular disease or disorder or is at risk for developing a vascular disease or disorder. Following obtaining an accurate diagnosis, an appropriate treatment regimen may be selected. The protocols of the present invention may also be used for evaluating a treatment regimen.

Optimization of treatment

In an embodiment of the present invention, the results of one or more imaging procedures, such as SPECT imaging procedures, are used to optimize a treatment. For some applications, the imaging procedures are performed using imaging protocols described herein, or in the co-assigned applications incorporated herein by reference. For some applications, a therapeutic radiopharmaceutical agent is administered at a low dose, and an imaging procedure, e.g., a SPECT imaging procedure, is performed, such as by using the imaging techniques described herein or in the co-assigned applications incorporated herein by reference, to determine information regarding the uptake of the radiopharmaceutical agent, such as areas in the body at which the radiopharmaceutical agent concentrates, levels of concentration of the radiopharmaceutical, actual bioavailability of the radiopharmaceutical, and kinetic information. This information is used in order to limit the toxicity of a subsequent administration of the radiopharmaceutical agent at a higher, therapeutic dose. For some applications, software calculates the maximum dose of radiopharmaceutical that can be delivered without exceeding the maximum accumulation of the

radiopharmaceutical in sensitive organs and/or tissues. The use of this technique thus enables treatment to be customized per patient, rather than relying on textbook curves of bioavailability applicable to large patient populations.

In an embodiment of the present invention, a therapeutic radiopharmaceutical agent is administered at a therapeutically-effective dose, and an imaging procedure, e.g., a SPECT imaging procedure, is performed, such as by using the imaging techniques described herein or in the co-assigned applications incorporated herein by reference, to determine the bioclearance of the radiopharmaceutical. Further treatment sessions are planned based on the determined bioclearance. For example, a subsequent administration of the therapeutic radiopharmaceutical is performed once the concentration of the initially administered dose falls below a certain level, e.g., in particular sensitive organs and/or tissues, and/or in the target organ and/or tissue. Alternatively, the therapeutic radiopharmaceutical agent is administered continuously in a closed loop at a rate determined responsively to the bioclearance of the radiopharmaceutical, as determined periodically or substantially continuously by imaging. For some applications, such continuous administration is configured to maintain a generally constant level of the radiopharmaceutical in the target organ or tissue, or another desired time curve of concentration.

In an embodiment of the present invention, a method for treating a patient comprises applying a therapy to the patient (either a drug therapy or a non-drug therapy), administering a radiopharmaceutical agent to the patient, performing a functional imaging procedure, e.g., a SPECT imaging procedure, on the patient to measure a property indicative of biochemical activity of at least one tissue of the patient, and modifying at least one parameter of the therapy responsively to the measured biochemical activity, typically to optimize the therapy and/or customize the therapy for the patient, either on a long- or short-term basis. For some applications, this technique is used to monitor: (a) a therapeutic effect of a therapy (e.g., an antibiotic or a chemotherapy agent) on target cells, tissue, or an organ, and/or (b) an undesired effect of the therapy on non-target cells, tissue, or organs. For some applications, such monitoring is performed by repeating the imaging procedure at least once per day, such as at least once per hour, at least once per minute, at least once per ten second period, or substantially continuously during administration of the therapy. The measured property of the tissue may include, for example, size,

perfusion, a marker of viability or apoptosis, an inflammatory process, metabolism, expression of specific proteins and/or mRNA, or cancer-specific activity. Modifying the parameter of the therapy may include, for example, increasing or decreasing dose, changing a cycle of the therapy, or changing a timing of the therapy. For some applications, the method comprises keeping records of the measured properties. For some applications, at least one parameter of the imaging process is customized, such as a parameter of the radiopharmaceutical (e.g., a dose), a parameter of image acquisition (e.g., timing), a parameter of administration of the radiopharmaceutical agent (e.g., timing of administration), or a parameter of image analysis.

The functional imaging procedure is typically a high sensitivity imaging procedure, e.g., a SPECT imaging procedure, which is typically performed using the imaging techniques described herein or in the co-assigned applications incorporated herein by reference. Such high sensitivity enables both the observation of the effect of the therapy on the target tissue, and adverse side effects of the therapy on non-target tissue. In addition, such high sensitivity enables the use of a low dose of the radiopharmaceutical agent, which allows the imaging procedure to be safely repeated a plurality of times, if necessary, without exceeding maximum radiation exposure limits. For some applications, the use of such high-sensitivity imaging procedures enables the monitoring of long-term processes ordinarily not detectible using cameras having conventional resolutions.

In an embodiment, the therapy includes administering a cocktail of drugs having differing respective therapeutic benefits and side effects. These techniques are used to determine doses and/or relative doses of the plurality of drugs in the cocktail, in order to achieve an optimized, customized balance between the benefits and side-effects of each of the drugs, for a specific patient or group of patients. In contrast, the relative doses of drugs in conventional cocktail therapies are typically pre-defined for all patients, rather than customized for each individual patient or group of patients.

A number of drugs suffer from lack of specificity because they do not sufficiently distinguish target cells from non-target cells when applied to an entire patient population. However, customization of the dose of such drugs for a particular patient enables the drugs to sufficiently distinguish target cells from non-target cells. For example, if a certain drug binds to target cells on average ten times more than it does to non-target cells, but the patient-to-patient variability is 50 times, it may be

impossible to determine a single recommended dose that would apply to all patients, and the drug thus may not receive regulatory approval. Using the techniques described herein, a precise dose of the drug is determined for the specific patient, which dose is high enough to be therapeutically effective in the specific patient, but as low as possible to avoid side effects for the specific patient. Alternatively or additionally, these techniques are used during a drug development process, a regulatory approval process, or thereafter to determine recommended doses for segments of a population upon which the drug has differing effects.

Reagents of the above-described protocols can be incorporated into a commercial kit or system for imaging as further described hereinbelow, detecting, and evaluating the herein described medical conditions such as cardiac plaques and tumors as described herein. In addition, reagent of the herein described protocols can be incorporated into a kit for determining myocardial perfusion in response to treatment measures. For example, the kit may contain radiopharmaceutical and pharmacological agents and instructions for use and may further contain directions on the administration and use of such agents in conjunction with the appropriate imaging technology and dosage requirement for the intended use.

Additional objects, advantages, and novel features of the present invention will become apparent to one ordinarily skilled in the art upon examination of the following examples, which are not intended to be limiting. Additionally, each of the various embodiments and aspects of the present invention as delineated hereinabove and as claimed in the claims section below finds experimental support in the following examples.

This application claims the benefit of:

- International Application PCT/IL2005/001215, filed November 16, 2005;
- International Application PCT/IL2005/001173, filed November 9, 2005,
- US Application 60/700,318, filed July 19, 2005;
- US Application 60/700,299, filed July 19, 2005;
- US Application 60/700,317, filed July 19, 2005;
- US Application 60/700,753, filed July 20, 2005;
- US Application 60/700,752, filed July 20, 2005;

- US Application 60/702,979, filed July 28, 2005;
- US Application 60/720,034, filed September 26, 2005;
- US Application 60/720,652, filed September 27, 2005;
- US Application 60/720,541, filed September 27, 2005,
- US Application 60/750,287, filed December 13, 2005;
- US Application 60/750,334, filed December 15, 2005;
- US Application 60/750,597, filed December 15, 2005;
- US Application 60/800,845, filed May 17, 2006;
- US Application 60/800,846, filed May 17, 2006;
- Israel Application 171346, filed October 10, 2005;
- Israel Application 172349, filed November 27, 2005;
- US Application 60/741,440, filed December 2, 2005;
- International Application PCT/IL2006/000059, filed January 15, 2006;
- US Application 60/763,458, filed January 31, 2006;
- International Application PCT/IL2006/000562, filed May 11, 2006; and
- US Application 60/799,688, filed May 11, 2006;
- US Application 60/816,970, filed June 28, 2006; and

Information of all of which is herein incorporated in entirety by reference.

This application further incorporates by reference all the information of the International Application entitled “RECONSTRUCTION STABILIZER AND ACTIVE VISION” which is being co-filed by the same assignee of the present invention on July 19, 2006.

EXAMPLES

Reference is now made to the following examples, which together with the above descriptions, illustrate the invention in a non limiting fashion.

EXAMPLE 1

Exemplary imaging protocols

Table 1

Description: A fast, dual isotope, imaging protocol
Indication: Myocardial perfusion

Length of time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
10 -15 min	Rest				
2 min	Imaging				
variable	Stress				Physical
	Peak stress injection	Tc 99m sestamibi	Medium dose for example 20-30	Bolus IV	
30-60 min	waiting				
2 min	Imaging				

Timeframe summary:
Total imaging time: 4 min.
Total patient time: 60-90 min.
Clinical protocol advantages: fast imaging time compared to standard imaging methods.

Table 2

Description: A fast, single isotope, imaging protocol
Indication: Myocardial perfusion

Length of time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tc 99m sestamibi	Low dose for example 8-10	Bolus IV	
30 min	rest				
2 min	imaging				
variable	Stress				physical
	Peak stress injection	Tc 99m sestamibi	Medium dose for example 20-30	Bolus IV	
30-60 min	waiting				

2 min	Imaging				

Timeframe summary:
Total imaging time: 4 min.
Total patient time: 60-90 min.
Clinical protocol advantages: Fast imaging time compared to standard imaging methods.

Table 3

Description: An ultra fast, dual isotope, imaging protocol
Indication: Myocardial perfusion

Length of time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*
	Injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
2 min	rest				
2 min	imaging				
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole
	Peak stress injection	Tc 99m sestamibi	Medium dose for example 20-30	Bolus IV	
2 min	Imaging				

Timeframe summary:
Total imaging time: 4 min.
Total patient time: 20-30 min.
Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Avoidance of liver radioactivity since imaging takes place substantially immediately after injection, before buildup of radioactivity in the liver takes place.

Table 4

Description: An ultra fast, single isotope, imaging protocol
Indication: Myocardial perfusion

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*
	Injection	Tc 99m sestamibi	low dose for examp	Bolus IV	

			le 8-10		
2 min	imaging				
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole
	Peak stress injection	Tc 99m sestamibi	Medium dose for example 20-30	Bolus IV	
2 min	Imaging				

Timeframe summary:
Total imaging time: 4 min.
Total patient time: 20-30 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Avoidance of liver radioactivity since imaging takes place substantially immediately after injection, before buildup of radioactivity in the liver takes place.

Table 5

Description : A dual isotope, simultaneous imaging protocol
Indication : Myocardial perfusion

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
15 min	rest				
2 min	imaging				
30-60 min	Stress				physical
	Peak stress injection	Tc 99m sestamibi	Medium dose for example 20-30	Bolus IV	
2 min	Imaging				

Timeframe summary:
Total imaging time: 2 min.
Total patient time: 45-90min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.

2. Dual registration of the two isotopes, when imaged simultaneously avoiding patient movement between acquisitions.

Table 6

Description: A fast, dual isotope, thallium-stress-perfusion, imaging protocol
Indication: Myocardial perfusion

Length of time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tc 99 sestamibi	Medium dose for example 20-30	Bolus IV	
15-30 min	Rest				
2 min	Imaging				
variable	Stress				Physical
	Peak stress injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
10-15 min	waiting				
4 min	Imaging				
4 hours	waiting				
6 min	imaging				

Timeframe summary:
Total imaging time: 6 min.
Total patient time: 45-60min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Better flow linearity.
3. Ability to detect small lesions
4. Ability to determine viability
5. High quality Thallium images

Table 7

Description: A fast, dual isotope, Tl-stress-perfusion, imaging protocol
Indication: Myocardial perfusion

Length of time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tc 99m sestamibi	low dose for example 3	Bolus IV	
15-30 min	Rest				
2 min	Imaging				
2 min	Stress			Infusion IV	Pharmacological - for

					example adenosine or dipyridamole
	Peak stress injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
4 min	Imaging				
4 hours	waiting				
6 min	imaging				

Timeframe summary:
Total imaging time: 6 min.
Total patient time: 20-30min. Additional redistribution time of 4 h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Better flow linearity.
3. Ability to detect small lesions
4. Ability to determine viability
5. High quality Thallium images

Table 8

Description: An ultra fast, dual isotope, thallium-stress-perfusion and redistribution, imaging protocol
Indication: Myocardial perfusion

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	Tc 99m sestamibi	low dose for example 3	Bolus IV	
2 min	Imaging				
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole
	Peak stress injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
4 min	Imaging				
4 hours	waiting				
6 min	imaging				

Timeframe summary:
Total imaging time: 6 min.
Total patient time : 10-20 min. Additional redistribution time of 4 h.
Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Better flow linearity.
3. Ability to detect small lesions
4. Ability to determine viability.
5. A single acquisition.
6. Dual registration of the two isotopes imaged simultaneously avoiding patient movement during acquisition.

Table 9

Description: A fast, dual isotope, simultaneous imaging protocol
Indication: Myocardial perfusion

Length of time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*
	Injection	Tc 99m sestamibi	low dose for example 3	Bolus IV	
30 min	Rest				
2 min	Imaging				
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole
	Peak stress injection	Tl 201 thallous chloride	Medium dose for example 3	Bolus IV	
2 min	Rest				
4 min	Imaging				

Timeframe summary:
Total imaging time: 6 min.
Total patient time: 10-20 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Single imaging time.
3. Better flow linearity.
4. Ability to detect small lesions
5. A single acquisition.
6. Dual registration of the two isotopes imaged simultaneously avoiding patient movement during acquisition.

Table 10

Description: A fast, single isotope, Tc 99m teboroxime imaging protocol
Indication: Myocardial perfusion

Length of time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*
	Injection	Tc 99m	Medium	Bolus IV	

		Teboroxime	dose for example 8-10		
2-10 min	Imaging				
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole
	Peak stress	Tc 99m Teboroxime	Medium dose for example 20-30	Bolus IV	
2-10 min	Imaging				

Timeframe summary:
Total imaging time: 12 min.
Total patient time: 20 min.
Clinical protocol advantages:
Fast imaging time compared to standard imaging methods.

Table 11

Description: Lung V/P –DTPA aerosol and macro-aggregated albumin (lung perfusion agent) protocol
Indication: for studying lung perfusion by quantitative parameters

Length of time	***Patient flow***	***Radiopharmaceutical***	***Patient relevant diagnosis (diabetes, BP, etc….)***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tc 99m DTPA		low dose for example Up to 5	Bolus IV	
	Injection	MAA		Low dose for example Up to 5 (up to 1Mparticles)	Bolus IV	
0-30 min	Imaging					Energy window 3-15%

Timeframe summary:
Total imaging time: 12 min.
Clinical protocol advantages:
Fast imaging time compared to standard imaging methods.

Table 12

Description: Fast MDP bone scan whole body scan protocol.

Indication: to look for bone cancers or inflammatory processes of the bone (e.g. osteomyelitis)

Length of time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tc 99m MDP	Medium dose for example 20-30	Bolus IV	
0-60 min	Waiting				
6 min	Imaging				Energy window 3-15%

Timeframe summary:
Total imaging time: 0-60 min.
Clinical protocol advantages:
Fast imaging time compared to standard imaging methods.

Table 13

Description: In 111 WBC scan protocol.
Indication: imaging of inflammatory processes

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 111 WBC	Medium dose for example 2-3	Bolus IV	
24 h	Waiting				
1 min	Imaging				Energy window 3-15%

Timeframe summary:
Total imaging time: 1 min.
Clinical protocol advantages:
Fast imaging time compared to standard imaging methods.

Table 14

Description: A low dose, dual isotope, myocardial perfusion imaging protocol
Indication: myocardial perfusion

Length of	***Patient***	***Radioph***	***Dose***	***Mode of***	***Type of***	***Acquisition***

Time	*flow*	*armaceutical*	*(mCi)*	*administration*	*stress*	*parameters (detector; windowing, etc.)*
	Injection	Tl 201 thallous chloride	low dose for example 0.3	Bolus IV		
10-15 min	waiting					
15 min	Imaging					Energy window 3-15%
variable	Stress				physical	
	Peak stress injection	Tc 99m sestamibi	low dose for example 3	Bolus IV		
30-60 min	Waiting					
15 min	Imaging					Energy window 3-15%

Timeframe summary:
Total imaging time: 30 min.
Total patient time: 90 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Low dose. 3. Better spectral resolution.

Table 15

Description: A low dose, single isotope, myocardial perfusion imaging protocol
Indication: myocardial perfusion

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tc 99m sestamibi	Low dose for example 0.3	Bolus IV		
15-30 min	waiting					
15 min	Imaging					Energy window 3-15%
variable	Stress				physical	
	Peak stress injection	Tc 99m sestamibi	Low dose for example 3	Bolus IV		

30-60 min	Waiting					
15 min	Imaging					Energy window 3-15%

Timeframe summary:
Total imaging time: 30 min.
Total patient time: 90 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Low dose.
3. better spectral resolution

Table 16

Description: A low dose, simultaneous dual isotope, imaging protocol
Indication: myocardial perfusion

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tl 201 thallous chloride	Low dose for example 0.3	Bolus IV		
variable	Stress				physical	
	Peak stress injection	Tc 99m sestamibi	Low dose for example 3-5	Bolus IV		
30-60 min	Waiting					
5-15 min	Imaging					Energy window 3-15%

Timeframe summary:
Total imaging time: 5-15 min.
Total patient time: 90 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Low dose.
3. Better spectral resolution
4. Better registration of rest and stress due to avoidance of patient movement

Table 17

Description: A low dose, dual isotope, fast imaging protocol
Indication: Myocardial perfusion

Length of	*Patient*	*Radioph*	*Dose*	*Mode of*	*Type of*	*Acquisition*

Time	*flow*	*armaceutical*	*(mCi)*	*administration*	*stress*	*parameters (detector; windowing, etc.)*
	Injection	Tl 201 thallous chloride	Low dose for example 0.3	Bolus IV		
2 min	waiting					
15 min	Imaging					Energy window 3-15%
2 min	Stress			Infusion IV	Pharmacological - for example adenosine or dipyridamole	
	Peak stress injection	Tc 99m sestamibi	Low dose for example 3	Bolus IV		
15 min	Imaging					Energy window 3-15%

Timeframe summary:
Total imaging time: 30 min.
Total patient time: 45 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Low dose.

Table 18

Description: A low dose, single isotope, breast cancer imaging protocol
Indication: Detection of breast cancer

Time Since previous step	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tc 99m sestamibi	Low dose for example 0.3	Bolus IV	
15-30 min	waiting				
15 min	Imaging				Energy window 3-15%

Timeframe summary:
Total imaging time: 25 min.
Total patient time: 30-45 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Low dose.
3. Better spectral resolution
4. High resolution breast cancer imaging

Table 19

Description: brain perfusion mapping protocol
Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Time Since previous step	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	Tc 99m exametazine (HMPAO)	Low dose for example Up to 3	Bolus IV		
	Injection	Tc 99m ECD	Low dose for example Up to 3	Bolus IV		
	Injection	I 123 isofetamine hydrochloride	Low dose for example Up to 5	Bolus IV		
1h	Waiting					
up to 30 min.	imaging				Energy window 3-15%	1.Mg/min/gr 2.Cerebral flow reserve in rest and stress 3. Parametric quantitation Identification of disease signature

ECD= N,N'(1'2-ethylenediyl)bis-L-cysteine diethyl ester
Timeframe summary:
Total patient time – Up to 1h
Clinical protocol advantages:
This protocol can show stroke and other brain pathologies at an early stage and the extent of the event in an accurate way.

Table 20

Description: brain perfusion mapping protocol
Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc 99m exametazine (HMPAO)	Low dose for example Up to 3	Bolus IV		
Up to 1h	Waiting					
0-30 min	imaging				Energy window 3-15%	Brain perfusion

Timeframe summary:
Total patient time – up to 1h
Clinical protocol advantages:
This protocol can show stroke and other brain pathologies at an early stage and the extent of the event in an accurate way.

Table 21

Description: brain perfusion mapping protocol
Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc 99m ECD	Up to 3	Bolus IV		
Up to 1h	Waiting					
0 -30 min	imaging				Energy window 3-15%	Brain perfusion

ECD= N, N'(1'2-ethylenediyl)bis-L-cysteine diethyl ester
Timeframe summary:
Total patient time: up to 1h
Clinical protocol advantages:
This protocol can show stroke and other brain pathologies at an early stage and the extent of the event in an accurate way.

Table 22

Description: brain perfusion mapping protocol

Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	I 123 isofetamine hydrochloride	High dose for example Up to 5	Bolus IV		
Up to 1h	Waiting					
0 - 30 min	imaging				Energy window 3-15%	Brain perfusion

Timeframe summary:

Total patient time – up to 1h

Clinical protocol advantages:

This protocol can show stroke and other brain pathologies at an early stage and the extent of the event in an accurate way.

Table 23

Description: Dynamic brain perfusion mapping protocol

Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc 99m exametazine (HMPAO)	Low dose for example Up to 3	Bolus IV		
0 -30 min	imaging				Energy window 3-15%; detectors sweep the brain every 10-15 seconds	1.Mg/min/gr 2.Cerebral flow reserve in rest and stress 3. Parametric quantitation Identification of disease signatrue

Timeframe summary:
Total patient time – up to 30min
Clinical protocol advantages:

1. This protocol can show stroke at an early stage and the extent of the event in an accurate way.
2. Provides quantitative measurements of blood flow
3. Provides disease signature

Table 24

Description: Dynamic brain perfusion mapping protocol

Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Time Since previous step	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	Tc 99m ECD	Low dose for example Up to 3	Bolus IV		
0-30 min	imaging				Energy window 3-15%; detectors sweep the brain every 10-15 seconds	1.Mg/min/gr 2.Cerebral flow reserve in rest and stress 3. Parametric quantitation Identification of disease signatrue

ECD= N,N'(1'2-ethylenediyl)bis-L-cysteine diethyl ester

Timeframe summary:
Total patient time – up to 30min

Clinical protocol advantages:

1. This protocol can show stroke at an early stage and the extent of the event in an accurate way.
2. Provides quantitative measurements of blood flow
3. Provides disease signature

Table 25

Description: Dynamic brain perfusion mapping protocol
Indication: Brain perfusion for the diagnosis of brain pathologies such as ischemia, stroke, and types of dementia

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	I 123 isofetamine hydrochloride	High dose for example Up to 5	Bolus IV		
0 -30 min	imaging				Energy window 3-15%; detectors sweep the brain every 10-15 seconds	1.Mg/min/gr 2.Cerebral flow reserve in rest and stress 3. Parametric quantitation Identification of disease signatrue

Timeframe summary:
Total patient time – up to 30min
Clinical protocol advantages:

1. This protocol can show stroke at an early stage and the extent of the event in an accurate way.
2. Provides quantitative measurements of blood flow
3. Provides disease signature

Table 26

Description: Dynamic hepatobiliary imaging
Indication: studying the structure of the liver including identification of hemangiomas, abscesses, and liver enlargement.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
0	Injection	Tc 99m mebrofenin	Low dose for example 0.5	Bolus IV		
30 min	imaging				Energy	1.Fluid flow

					window 3-15%; detectors sweep the region of interest every 10-15 seconds	2. rate of tracer uptake (passive or active) 3. accumulation and redistribution of tracer 4. tracer metabolism 5. secretion and or washout of tracer or metabolite (passive or active)

Timeframe summary:
Total imaging time: 30 min.
Total patient time: 30 min.

Table 27

Description: lung V/P DTPA aerosol and macro aggregated albumin (lung perfusion agent) protocol)
Indication: for studying lung perfusion

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tc 99m DTPA	Low dose for example Up to 3 (up to 1M particles)	Bolus IV	
	Injection	MAA or DTPA In 111	Up to 0.5	Bolus IV	
6 min	imaging				Energy window 3-15 %

Timeframe summary:
Total imaging time: 6min.
Total patient time: 6 min.
Clinical protocol advantages:
Fast imaging time compared to standard imaging methods.

Table 28

Description: Dynamic myocardial perfusion (thallium rest) protocol
Indication: imaging of cardiac perfusion under rest conditions

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	Tl 201 thallous chloride	High dose for example 4	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
2-20 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	

Timeframe summary:
Total imaging time: 2-20 min.
Total patient time: 2-20 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 29

Description: Dynamic cardiac perfusion (thallium stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Time Since previous step	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
Variable	Stress			Infusion IV	Physical or pharmacological - for example adenosine or dipyridamole		

	Injection at peak stress	Tl 201 thallous chloride	High dose for example 4	Bolus IV			
2-20 min	imaging					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:
Total imaging time – 2-20 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 30

Description: Dynamic cardiac perfusion (teboroxime rest) protocol
Indication: imaging of cardiac perfusion under rest conditions

Length of time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	Teboroxime	medium dose for example 30	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
15 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	

Timeframe summary:
Total imaging time: 2-20 min.

Total patient time: 2-20 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 31

Description: Dynamic cardiac perfusion (teboroxime stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Length of Time	*Patient flow*	*Radio Pharma ceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
variable	Stress				Physical or pharmaco logical - for example adenosine or dipyridamole		
	Injection at peak stress	Teboroxime	Low dose for example 4	Bolus IV			
2-20 min	imaging					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:
Total imaging time – 2-20 min.
Total patient time – 2-20 min.

Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 32

Description: Dynamic cardiac perfusion (sestamibi rest) protocol
Indication: imaging of cardiac perfusion under rest conditions

Length of time	*Patient flow*	*Radioph armaceu*	*Dose (mCi*	*Mode of adminis*	*Acquisitio n*	*Clinical parameters*

		tical	*)*	*tration*	*parameters (detector; windowing , etc.)*	*acquired after processing*
	Injection	Tc 99m sestamibi	Medium dose for example 30	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
15 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 33

Description: Dynamic cardiac perfusion (sestamibi stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Length of time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
Variable	Stress			Infusion IV	Physical or pharmacological - for example adenosine or dipyridamole		
	Injection at peak	Tc 99m sestamibi	Medium dose	Bolus IV			

	stress		for exampl e 30				
15 min	imagin g					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitatio n

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 34

Description: Dynamic cardiac perfusion (tetrofosmin rest) protocol
Indication: imaging of cardiac perfusion under rest conditions

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	tetrofosmin	Medium dose for example 30	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
15 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 35

Description: Dynamic cardiac perfusion (tetrofosmin stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
variable	Stress			Infusion IV	Physical or pharmacological - for example adenosine or dipyridamole		
	Injection at peak stress	tetrofosmin	Medium dose for example 30	Bolus IV			
15 min	imaging					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 36

Description: Dynamic cardiac perfusion (Q12 rest) protocol
Indication: imaging of cardiac perfusion under rest conditions

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc 99m sestamibi	Medium dose for example 30	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
15 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 37

Description: Dynamic cardiac perfusion (Q12 stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
Variable	Stress			Infusion IV	Physical or pharmacological - for example adenosin		

					e or dipyridamole		
	Injection at peak stress	Tc sestamibi	Medium dose for example 30	Bolus IV			
15 min	imaging					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 38

Description: cardiac perfusion (BMIPP rest) protocol
Indication: Dynamic imaging of cardiac perfusion under rest conditions

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc 99m sestamibi	Medium dose for example 30	Bolus IV		1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation
15 min	Imaging				Energy window 3-15%; detectors sweep the region of interest.	

					every 10-15 seconds	

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 39

Description: Dynamic cardiac perfusion (BMIPP stress) protocol
Indication: imaging of cardiac perfusion under stress conditions

Length of Time	*Patient flow*	*Radiop harmac eutical*	*Dos e (mC i)*	*Mode of administrati on*	*Type of stress*	*Acquisiti on paramete rs (detector ; windowi ng, etc.)*	*Clinical parameter s acquired after processing*
variable	Stress			Infusion IV	Physical or pharmac ological - for example adenosin e or dipyrida mole		
	Injectio n at peak stress	Tc sestami bi	Med ium dose for exa mpl e 30	Bolus IV			
15 min	imagin g					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitatio n

Timeframe summary:
Total imaging time: 15 min.
Total patient time: 15 min.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 40

Description: Dynamic cardiac perfusion protocol

Indication: imaging of cardiac perfusion under stress or rest conditions

Length of time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
Variable	Stress or rest			Infusion IV	Physical or pharmacological - for example adenosine or dipyridamole		
	Injection at peak stress	Any radiopharmaceutical	Medium dose for example 30	Bolus IV			
10 min	imaging					Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:

Total imaging time: 10 min.

Total patient time: 10 min.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 41

Description: Dynamic cardiac perfusion protocol utilizing PET pharmaceuticals within the currently used PET protocols.

Indication: imaging of cardiac perfusion under stress or rest conditions

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Rest injection	Any PET radiopharmaceutical	Medium dose for example 30	Bolus IV		
Up to 15 minutes	Imaging				Energy window 3-15%	1. Ml/min/gr 2. coronary flow reserve 3. parametric quantitation

Timeframe summary:

Total imaging time: 10 min.

Total patient time: 10 min.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 42

Description: Cancer – dynamic single isotope tumor perfusion protocol under rest or stress.

Indication: Diagnosis and evaluation of tumors

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	injection	Teboroxime Tc 99m or Tc 99m sestamibi or Tl 201 or Tc 99m tetrofosmin	Medium dose for example 30mCi Tc or high dose for example 4mCi Tl	Bolus IV		
Up to 5 min	Imaging				Energy	1.

					window 3-15%; detectors sweep the region of interest every 10-15 seconds	quantitative parameters (Ml/min/gr) 2. parametric quantitation

Timeframe summary:
Total imaging time: 5 min.
Total patient time: 5 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.
3. Tumor blood flow measurements
4. Accurate tumor diagnosis
5. Evaluation of multi drug resistance
6. Monitoring of treatment response

Table 43

Description: Cancer – Dynamic simultaneous dual isotope tumor perfusion protocol under rest or stress.
Indication: Diagnosis and evaluation of tumors by simultaneous dual isotope.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	injection	Tl 201 thallous chloride and Tc 99m sestamibi	High dose for example Tl -4 Medium doe for example Tc- up to 30	Bolus IV		
Up to 5 min	Imaging				Energy window 3-15%; detectors sweep the region of interest.	1. quantitative parameters (Ml/min/gr) 2. parametric quantitation

					every 10-15 seconds	

Timeframe summary:
Total imaging time: 5 min.
Total patient time: 5 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.
3. Blood flow measurements
4. Accurate tumor diagnosis
5. Evaluation of multi drug resistance
6. Monitoring of treatment response

Table 44

Description: kidney –Dynamic renal function protocol.
Indication: assessment of filtration and tubular secretion, perfusion and secretion.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	Tc99m DTPA and Tc 99m-MAG3	low dose for example - Tc99m DTPA – 1 Tc MAG 3 – 10	Bolus IV		
10 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. quantitative parameters (Ml/min/gr) 2. parametric quantitation

Timeframe summary:
Total imaging time – 10min.
Total patient time – 10 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.

2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 45

Description: Dynamic renal function protocol.
Indication: assessment of filtration and tubular secretion, perfusion and secretion.

Time Since previous step	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	Tc99m DTPA and Hippuran I-123	Low dose for example 1 each	Bolus IV		
10 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. quantitative parameters (Ml/min/gr) 2. parametric quantitation

Timeframe summary:
Total imaging time: 10min.
Total patient time: 10 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 46

Description: Dynamic brain perfusion protocol.
Indication: perfusion mapping under rest or pharmacological stress conditions

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*	*Clinical parameters acquired after processing*
	Injection	HMPAO 99m labeled Tc 99m ECD (neurolit	Medium dose for example	Bolus IV		

		e) Spectamine I 123	20 Low dose for example. Up to 5	Bolus IV		
Up to 30 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds	1. quantitative parameters (Ml/min/gr) 2. cerebral flow reserve 3. parametric quantitation 4. disease signature

Timeframe summary:
Total imaging time: 30min.
Total patient time: 30 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 47

Description: Dynamic brain perfusion protocol.
Indication: perfusion mapping under rest or pharmacological stress conditions

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***	***Clinical parameters acquired after processing***
	Injection	teboroxime	Low dose for example Up to 20	Bolus IV		
Up to 30 min	Imaging				Energy window 3-15%; detectors sweep the region of interest	1. quantitative parameters (Ml/min/gr) 2. cerebral flow reserve 3. parametric

					every 10-15 seconds	quantitation 4. disease signature

Timeframe summary:
Total imaging time: 30min.
Total patient time: 30 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 48

Description: hepatobiliary protocol
Indication: liver structure (hemangiomas, abscesses, liver enlargement, etc.)

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tc 99m sulfur colloid	low dose for examp le Up to 5	Bolus IV	
Up to 10 min	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 10min.
Total patient time: 10 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 49

Description: liver function study rest or stress protocol
Indication: Pathological liver function

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector;*

					windowing, etc.)
	Injection	Tc 99m disida (disulfenine , or chole tec),	Up to 10	Bolus IV	
5 min ' Every 5 minutes up to an hour	Imaging				Energy window 3-15%; detectors sweep the region of interest every 10-15 seconds
	Injection of agent for gall bladder contraction Only if no activity is seen in the intestine after 1 hour of imaging				

Timeframe summary:
Total imaging time: 1h.
Total patient time: 1h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the study of fluid flow, rate of tracer uptake (passive or active), tracer accumulation and redistribution, tracer metabolism, and secretion and/or washout (active or passive) of tracer/metabolites.

Table 50

Description: dual phase gastric emptying study protocol
Indication: determining the rate the stomach empties of food

Length of time	*Patient flow*	*Radiopharma ceutical*	*Dose (mCi)*	*Mode of administration*
	Ingestion of labeled food	Solid food labled with Tc 99m S colloidor or liquid food labeled with IN 111 DTPA	Medium dose for example 3MBq solid 0.5 MBqliqu id	PO
Until the stomach is approximately empty of all tracer	Imaging			

Clinical protocol advantages: dynamic SPECT imaging for increased resolution

Table 51

Description: Cardiac vulnerable plaque study protocol

Indication: for identifying plaque in blood vessels that may be released in the blood stream and initiate a CVA or cardiac infarct

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***
	Injection	Annexin labeled with Tc99m	low dose for example Up to 5	Bolus IV
	Injection	AccuTec labeled with Tc 99m	low dose for example Up to 5	Bolus IV
24h	waiting			
30min	imaging			

Timeframe summary:
Total imaging time: 1h.
Total patient time: 1h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. The AccuTec attaches to activated platelets and shows thrombus. The Annexin attaches to apoptotic cells. Apoptotic cells being human neutrophils that have died and broken up demonstrating inflammatory infiltrate. The protocol enables the study of dynamic plaques that are associated with cardiac plaque tissue damage and repair.

Table 52

Description: Prostate imaging study protocol

Indication: determining the presence and/or extent of metastatic and/or primary cancer in the prostate.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***
	Injection	Prostascint containing 111 In DTPA	high dose for example Up to 5	
24-72h	waiting		Up to 10	Bolus IV
up to 60 min	imaging			

Timeframe summary:
Total patient time: 24-72h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. enables the study of dynamic plaques that are associated with tissue damage and repair.

Table 53

Description: SST receptor imaging study protocol

Indication: for determining the presence and/or extent of SST receptor expressing tumors, whether metastatic and/or primary cancerous tumors.

Length of Time	*Patient flow*	*Radiopharma ceutical*	*Dose (mCi)*	*Mode of administration*
	Injection	Octreotide containing 111 In DTPA	high dose for example Up to 5	Bolus IV
24h	waiting			
up to 60 min	Imaging			

Timeframe summary:

Total patient time: 24h.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. enables the study of SST receptor expressing tumors metastatic and/or primary cancerous tumors.

Table 54

Description: neuroendocrine tumors imaging study protocol.

Indication: for determining the presence and/or extent of metastatic and/or primary neuroendocrine tumors by binding t associated somatostatin receptors.

Length of Time	*Patient flow*	*Radiopharma ceutical*	*Dose (mCi)*	*Mode of administration*
	Injection	Neotec labeled withTc 99m	low dose for example Up to 20	Bolus IV
1h	waiting			
up to 30 min	Imaging			

Timeframe summary:

Total patient time – 1h.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. enables the study of neuroendocrine tumors.

Table 55

Description: Thrombus detection imaging study protocol.

Indication: for imaging DVT and intraarterial thrombusin coronary and carotid arteries, by binding to GP IIb/IIIa.

Length of Time	*Patient flow*	*Radiopharma ceutical*	*Dose (mCi)*	*Mode of administration*
	Injection	Acutec labeled with Tc 99m	low dose for example Up to 20	Bolus IV

0-20 min	waiting			
up to 60 min	Imaging			

Timeframe summary:
Total patient time – 20 min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. enables the study of thrombus detection including DVT and intraarterial thromus in coronary and carotid arteries.

Table 56

Description: Pheochromocytoma and or myocardial failure imaging study protocol.
Indication: for imaging pancreatic adrenergic tissue uptake and presynaptic adrenergic receptors, adrenergic being associated with adrenaline bu binding to GP IIb/IIIa receptors on platelets.

Length of Time	***Patient flow***	***Radiopharma ceutical***	***Dose (mCi)***	***Mode of administration***
	Injection	MIBG containing I 123 iofetamine hydrochloride	high dose for example Up to 5	Bolus IV
24h	waiting			
up to 30 min	Imaging			

Timeframe summary:
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. enables the study of tissue and receptors that are associated with adrenergic uptake.

Table 57

Description: Dynamic gated cardiac stress imaging protocol
Indication a dynamic study to investigate the effects of stress for example adenosine or dipyridamole, ice water and/or vasodilatation agents, on blood flow kinetics.

Length of Time	***Patient flow***	***Radioph armaceut ical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tl 291 thallous chloride	high dose for exam ple 4	Bolus IV		
0-2 min	waiting					
2-5 min	imaging					
	Stress injection			Bolus IV	For example adenosine	

					or dipyridamole and/or vasodilatation agents or hand in submerged into icewater	
0-5 min	waiting					
2-10 min	imaging					detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 15min.
Total patient time: 20min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. enables the investigation of the effects of stress on blood flow kinetics

Table 58

Description: a kidney function imaging protocol
Indication: a dynamic study to investigate the effects of stress on blood flow kinetics of the kidneys.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Type of stress***
	Injection	DTPA and/or Tc MAG3	low dose for example 2-4	Bolus IV	
	Stress injection			Bolus IV	captopril, fuside and/or vasodilatation or diuretic agents or hand in submerged into icewater
10-30 min	Imaging				

Timeframe summary:
Total imaging time: 32min.
Total patient time: 1h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the investigation of the effects of stress on blood flow kinetics (captopril, fuside etc.) of the kidney.

Table 59

Description: Bexaar dosimetry imaging protocol

Indication: a study to determine the dose required to inject in order to administer an effective dose of 75 REM.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters. (detector; windowing, etc.)*
	Injection	I123 iofetamine hydrochloride	5Mci/ 35 mg	Bolus IV	
5 min	Imaging				Energy window 3-15%

3 acquisitions are acquired during the week to produce a graph of metabolism.

Timeframe summary per scan:
Total imaging time: 5min.
Total patient time: 5h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables the determination of the dose required to inject in order to administer an effective dose of 75 REM.

Table 60

Description: Multi isotope combination protocol

Indication: parathyroid adenoma imaging and anatomical differentiation of the parathyroid from the thyroid.

Length of time	*Patient flow*	*Radiopharmaceutical*	*remarks*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Thallium 201 thallous chloride	Parathyroid avid agent	low dose for example 1	Bolus IV	
	Injection	Tc 99m pertechnetate	Thyroid agent	low dose for example 15	Bolus IV	
10 min	Waiting					
5 min	imaging					Energy window 2-10%;

Timeframe summary:

Total imaging time: 5min.
Total patient time: 15min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables parathyroid adenoma imaging and anatomical differentiation of the parathyroid from the thyroid.

Table 61

Description: Multi-isotope combination protocol
Indication: parathyroid adenoma imaging and anatomical differentiation of the parathyroid from the thyroid.

Length of time	*Patient flow*	*Radiopharmaceutical*	*remarks*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection.	Tc 99m sestamibi	Parathyroid avid agent	low dose for example 15	Bolus IV	
	Injection	I 123	Thyroid agent	low dose for example 100μCi	Bolus IV	
10 min	Waiting					
5 min	imaging					Energy window 2-10%

Timeframe summary:
Total imaging time: 5min.
Total patient time: 15min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables parathyroid adenoma imaging and anatomical differentiation of the parathyroid from the thyroid.

Table 62

Description: Multi-isotope combination protocol
Indication: imaging of thyroid cancer identification of the location of the thyroid cancer.

Length of Time	*Patient flow*	*Radiopharmaceutical*	*remarks*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tc 99m	Bone	low	Bolus IV	

		MDP	imaging agent	dose for example 10		
	Injection	Tl201 thallium chloride	Thyroid agent	high dose for example 4	Bolus IV	
2h	Waiting					
30 min	imaging					Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 2h and 30min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. imaging of thyroid cancer identification of the location of the thyroid cancer. Tc 99m MDP enables visualization of the skeleton to provide anatomical landmarks. Tc 99m labeling of red blood cells enables the larger blood vessels to be visualized to provide anatomical landmarks.

Table 63

Description: Multi-isotope combination protocol
Indication: localization of certain endocrine tumors.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 111 octeotride	Possible to administer simultaneously	High dose for example 4	Bolus IV	
	Injection	Tc 99m MDP		low dose for example 15	Bolus IV	
Up to 2 h	waiting					
30 min	imaging					Energy window 2-10%

* Imaging may be done within 3 days of injection of In 111 octeotride but within 2h after injection of Tc 99m MDP

* 3. In 111 Octeotide and Tc 99m MDP may be administered in combination to optimally localize certain endocrine tumors. In 111 octeotide is a tumor imaging agent

for somastatin receptor expressing tumors. Tc 99m MDP is a bone imaging agent which enables visualiziation of the skeleton to provide anatomical landmarks.

Timeframe summary:

Total imaging time: 30min.

Total patient time: 2h and 30min.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. localization of certain endocrine tumors.

Table 64

Description: Multi-isotope combination protocol

Indication: localization of certain endocrine tumors.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 111 octeotride	* It is Possible to administer simultaneously	high dose for example 4	Bolus IV	
Up to 3 days	waiting					
	Injection	Tc 99m MDP		low dose for example 15	Bolus IV	
Up to 2 hours	waiting					
30 min	imaging					Energy window 2-10%

* Imaging may be done within 3 days of injection of In 111 octeotride but within 2h after injection of Tc 99

* 3. In 111 Octeotide and Tc 99m MDP may be administered in combination to optimally localize certain endocrine tumors. In 111 octeotide is a tumor imaging agent for somastatin receptor expressing tumors. Tc 99m MDP is a bone imaging agent which enables visualiziation of the skeleton to provide anatomical landmarks.

Timeframe summary:

Total imaging time: 30min.

Total patient time: 3 days.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. localization of certain endocrine tumors.

Table 65

Description: Multi-isotope combination protocol

Indication: delineating vascular structures of the pelvis or abdomen to differentiate from prostate cancer

Length of Time	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 111 capromab pentitde	* It is Possible to administer simultaneously	medium dose for example 3	Bolus IV	
Up to 3 days	waiting					
	Injection	Tc 99m RBCs		low dose for example 15	Bolus IV	
2 hours	waiting					
30 min	imaging					Energy window 2-10%

* Imaging may be done within 3 days of injection of In 111 capromab penticde but within 2h after injection of Tc 99m RBCs.

Timeframe summary:

Total imaging time: 30min.

Total patient time: 30 min to 3 days.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables the clinician to distinguish the blood vessels from the lymph nodes in the pelvis or abdomen.

Table 66

Description: Multi-isotope combination protocol

Indication: identification and localization of bone infection.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 111 WBC	* It is Possible to administer simultaneously	medium dose for example 3	Bolus IV	
Up to 3 days	waiting					
	Injection	Tc 99m		low	Bolus IV	

		colloid		dose for example 15		
2 hours	waiting					
30 min	imaging					Energy window 2-10%

* Imaging may be done within 3 days of injection of In 111 WBC but within 2h after injection of Tc 99m colloid.
Timeframe summary:
Total imaging time: 30min.
Total patient time: 30 min to 3 days.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Identification and localization of bone infection.

Table 67

Description: Multi-isotope combination protocol
Indication: Evaluation of invasion of bone or cartilage by head or neck cancer.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tl 201 thallous chloride	* It is Possible to administer simultaneously	Medium dose for example 2	Bolus IV	
	Injection	Tc 99mMDP		low dose for example 15	Bolus IV	
2h	Waiting					
30 min	imaging					Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 2h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Evaluation of invasion of bone or cartilage by head or neck cancer.

Table 68

Description: Dynamic multi-isotope combination protocol for multiple pathologies:
Indication: assessment of various pathological conditions, including cardiac, tumors and infection

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	In 11 WBCs	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tl 201 thallous chloride	low dose for example 1	Bolus IV	
	Injection	Tc 99m sestamibi	low dose for example 10	Bolus IV	
3min	Waiting				
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 25h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Assessment of various pathological conditions, including cardiac, tumors and infection with only one acquisition
3. Easy registration as a result of simultaneous imaging

Table 69

Description: Dynamic multiple isotope combination protocol for different pathological processes of the same organ
Indication: study of acute myocardial ischemia

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Patient relevant diagnosis (diabetes, BP,*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*

			etc....)			
	Injection	I 123 BMIPP		low dose for example 2	Bolus IV	
48h	Waiting					
	Injection	Tl 201 thallous chloride		low dose for example 1	Bolus IV	
	Injection	Tc 99m sestamibi or Tc 99m teboroxime		low dose for example 10	Bolus IV	
30 min	imaging					Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 48h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. study of acute myocardial ischemia
3. BMIPP identifies the ischemic / infracted area while the other isotopes identify the perfused area; simultaneous imaging provides a more accurate means of identifying myocardial perfusion pathologies

Table 70

Description: combination protocol for different pathological processes of the same organ
Indication: fever of unknown origin

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	In 11 WBC	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m Fanoselom	low dose	Bolus IV	

		ab	for example 15		
30 min	imaging				Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. study of fever of unknown origin
3. Differential diagnosis in one scan

Table 71

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ
Indication: schizophrenia or Parkinson's disease.

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
-	Injection	I 123 IBZM	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m HMPAO	low dose for example 15	Bolus IV	
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. study of schizophrenia or Parkinson's disease.
3. Mapping of brain activity in different pathological states.

Table 72

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ

Indication: tumor identification and characterization by perfusion studies.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	In 111 WBC	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m sestamibi or Tc 99m Arcitumo Mab Or Tl 201 thallous chloride	low dose for example Tc – 10 Tl – 1	Bolus IV	
5min	Waiting				
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:

Total imaging time – 30min.

Total patient time –24h.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Tumor identification and characterization by perfusion studies.
3. Differentiation between tumors and inflammation
4. Accurate registration due to simultaneous imaging of all isotopes
5. Differential diagnosis in one scan

Table 73

Description: combination protocol for different pathological processes of the same organ.

Indication: Dynamic flow studies for the investigation of renal function.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	In 111	low	Bolus IV	

		DTPA	dose for examp le 2		
24h	Waiting				
	Injection	Tc 99m MAG3	low dose for examp le 15	Bolus IV	
5min	Waiting				
30 min	imaging				Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Dynamic flow studies for the investigation of renal function.

Table 74

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ
Indication: Tumor perfusion and therapeutic response.

Length of Time	***Patient flow***	***Radiophar maceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tl thallous chloride	low dose for examp le 1	Bolus IV	
	Injection	Tc 99m teboroxime or Tc 99m sestamibi	low dose for examp le 15	Bolus IV	
1h	Waiting				
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 1h.

Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Tumor perfusion and therapeutic response determined by absolute blood flow to and from tumor
3. Determination of multi-drug resistance by measurement of washout

Table 75

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ
Indication: tumor perfusion and therapeutic response.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tl thallous chloride	low dose for example 1	Bolus IV	
	Injection	Tc 99m Annexin	low dose for example 15	Bolus IV	
1h	Waiting				
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 1h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Tumor perfusion with thallium and therapeutic response by monitoring apoptosis with annexin

Table 76

Description: Multi-isotope combination protocol for different pathological processes of the same organ
Indication: Differentiation between infection and bone marrow activation.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*

	Injection	In 111 WBC	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m sulfur colloid	low dose for example 15	Bolus IV	
30 min	imaging				Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Differentiation between infection and bone marrow activation
3. Differential diagnosis with one scan

Table 77

Description: Muti-isotope combination protocol for different pathological processes of the same organ
Indication: Differentiation between acute and chronic osteomyelitis.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	In 111 WBC	low dose for example 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m MDP	low dose for example 15	Bolus IV	
30 min	imaging				Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time: 24h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Differentiation between acute and chronic osteomyelitis

3. Differential diagnosis in one scan

Table 78

Description: Multi-isotope combination protocol for different pathological processes of the same organ

Indication: Differentiation between acute and chronic inflammation.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Gallium 67	low dose for examp le 5	Bolus IV	
	Injection	In 111 WBCs	high dose for examp le 15	Bolus IV	
72h	Waiting				
30 min	imaging				Energy window 2-10 %

Timeframe summary:
Total imaging time: 30min.
Total patient time: 72h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Differentiation between acute and chronic inflammation.
3. Differential diagnosis in one scan

Table 79

Description: Multi-isotope combination protocol for different pathological processes of the same organ

Indication: Study myocardial perfusion and apoptosis.

Length of Time	*Patient flow*	*Radiophar maceutical*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	In111 annexin	low dose for examp le 2	Bolus IV	
24h	Waiting				
	Injection	Tc 99m teboroxime or Tl 201 thallous	low dose for examp	Bolus IV	

		chloride	le Tc - 15 or medium dose for example Tl – 2		
0-3min	Waiting				
30 min	imaging				Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 25h.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Study myocardial perfusion and apoptosis.

Table 80

Description: Multi-isotope combination protocol for different pathological processes of the same organ
Indication: Investigation of myocardial perfusion and infarct

Length of Time	***Patient flow***	***Radiopharmaceutical***	***Dose (mCi)***	***Mode of administration***	***Acquisition parameters (detector; windowing, etc.)***
	Injection	Tl 201 thallous chloride	medium dose for example 2	Bolus IV	
	Injection	Tc 99m pyrophosphate	low dose for example 15	Bolus IV	
1h	Waiting				
30 min	imaging				Energy window 2-10%

Timeframe summary:
Total imaging time: 30min.
Total patient time:72h.

Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. investigation of myocardial perfusion and infarct

Table 81

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ
Indication: Investigation of myocardial perfusion and infarct

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Patient relevant diagnosis (diabetes, BP, etc....)*	*Dose (mCi)*	*Mode of administration*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	Tl 201 thallous chloride		medium dose for example 2	Bolus IV	
	Injection	Tc 99m pyrophosphate		low dose for example 15	Bolus IV	
30 min	imaging					Energy window 2-10%; detectors sweep the region of interest every 10-15 seconds

Timeframe summary:
Total imaging time: 30min.
Total patient time: 30min.
Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. investigation of myocardial perfusion and infarct

Table 82

Description: Dynamic multi-isotope combination protocol for different pathological processes of the same organ
Indication: Cardiac vulnerable plaque and myocardial perfusion study protocol

Length of Time	*Patient flow*	*Radiopharmaceutical*	*Dose (mCi)*	*Mode of administration*	*Type of stress*	*Acquisition parameters (detector; windowing, etc.)*
	Injection	*In 111	high	Bolus IV		

		annexin	dose for example 5			
24h	Waiting					
	Injection	**Tc 99m AccuTec	low dose for example 5	Bolus IV		
	Pharmacological stress			infusion IV	For example adenosine or dipyridamole vasodilatation	
2 min	Injection	Tl 201 thallous chloride	low dose for example 1	Bolus IV		
30 min	imaging					Energy window 2-10%

**AccuTec attaches to activated platelets and shows thrombus.

*Annexin attaches to apoptotic cells. Apoptotic cells being human neutrophils that have died and broken up, demonstrate inflammatory infiltrate.

Timeframe summary:

Total imaging time: 30min.

Total patient time: 25h.

Clinical protocol advantages:

1. Fast imaging time compared to standard imaging methods.
2. Enables identification of intra vascular plaque that may be released into the blood stream and as a result initiate a CVA or cardiac infarct.
3. Enables identification of the perfusion defect if any that is caused by these events.
4. Enables the study of dynamic plaques that are associated with cardiac plaque tissue damage and repair.

Table 83

Description: Non coincidence imaging using PET radiopharmaceuticals

Indication: study of glucose metabolism of cells including tumor, heart and brain cells.

Time Since previous step	***Patient flow***	***Radiopharmaceutical***	***remarks***	***Dose (mCi)***
	Injection	FDG as a substrate for hexokinase in glucose metabolism		30-50
up to 60 min	imaging			

Clinical protocol advantages:
1. Fast imaging time compared to standard imaging methods.
2. Enables study of glucose metabolism of cells including tumor, heart and brain cells using PET radiopharmaceuticals.

Protocols for Non-Coincidence Imaging Using PET Radiopharmaceuticals

The following imaging protocols use non-coincidence imaging using PET radiopharmaceuticals.

1. Use of F-18-Fluorodeoxyglucose (FDG), as a substrate for hexokinase in glucose metabolism, for the study of glucose metabolism of cells including tumor, heart and brain cells.

2. Use of F-18-Fluoromisonidazole for imaging of hypoxia and oxidative metabolism, with the clinical application of radiotherapy treatment planning.

3. Use of F-18-3'-Fluoro-3'-deoxythymidine (FLT) for the study of DNA synthesis.

4. Use of F-18-Fluoromethyl choline (FCH) as a choline precursor for cell membrane synthesis, for the study of choline metabolism of tumors.

5. Use of F-18-4-Fluoro-m-tyrosine (FMT) as a precursor for dopamine synthesis and as a substrate for aromatic amino acid decarboxylase (AAAD), with the clinical application of imaging brain tumors.

6. Use of F-18-6-Fluoro-L-DOPA as a precursor for dopamine synthesis and as a precursor for AAAD, with the clinical applications of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

7. Use of F-18-FP-β-CIT for binding to the dopamine transporter in dopaminergic axons, with the clinical application of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

8. Use of F-18-Pencyclovir (FHBG) to target thymidine kinase, with the clinical application of imaging reporter gene expression.

9. Use of F-18-Fuoroestradiol (FES) to target estrogen receptors, with the clinical application of breast tumor imaging.

10. Use of C-11-Methionine to target amino acid synthesis, with the clinical application of imaging brain tumors.

11. Use of Tc-99m-P280, Acutect® to target GP IIb/IIIa receptors on platelets, with the clinical applications of detection of thrombosis, such as deep vein thrombosis (DVT) and intratererial thrombosis in coronary and carotid arteries.

17. Use of C-11-Raclopride to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

18. Use of I-123-iodobenzamide (IBZM) to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

19. C-11-carfentanil to target Mu opioid receptors in brain, with the clinical application of imaging drug addiction.

20. Use of C-11-α-methyl-L-tryptophan as a precursor for α-methyl serotonin synthesis and as a substrate for AAAD enzyme, with the clinical application of imaging depression.

21. Use of C-115-Hydroxytryptophan as a precursor for serotonin synthesis with the clinical application of imaging neuroendocrine tumors.

22. Use of F-18-MPPF to bind to 5-HT1A (5-hydroxytryptamine-1A) serotonin receptors, with the clinical application of imaging depression and epilepsy.

23. Use of F-18-Altanserin to bind to 5-HT2A serotonin receptors with the clinical application of imaging depression and epilepsy.

24. Use of C-11-Acetate for the study of tricarboxylic acid cycle activity and oxidative metabolism with the clinical application of studying myocardial oxygen metabolism.

25. Use of C-11-Palmitate as a precursor for fatty acid metabolism with the clinical application of imaging myocardial metabolism.

26. Use of F-18-Fluorodopamine to target presynaptic adrenergic receptors

Table 84

	Short	***Medium***	***Long***
Heart	Up to 2 min	2-20 min	Over 20 min
Lung	Up to 30 min	30-60 min	Over 60 min
Breast	Up to 2 min	2-15 min	Over 15 min
Brain	Up to 2 min	2-20 min	Over 20 min
Liver	Up to 5 min	5-10 min	Over 10 min
Kidney	Up to 10 min	10-30 min	Over 30 min
Stomach	Up to 10 min	10-30 min	Over 30 min
Prostate	Up to 10 min	10-30 min	Over 30 min
Adrenal	Up to 10 min	10-30 min	Over 30 min
Thyroid	Up to 10 min	10-30 min	Over 30 min
Parathyroid	Up to 5 min	5-10 min	Over 10 min
Bone	Up to 10 min	10-30 min	Over 30 min

Table 85

	short	*medium*	*long*
Whole body	Up to 5 min	5-30 min	Over 30 min
SST receptor expression	Up to 5 min	5-10 min	Over 10 min
Endocrine tumors	Up to 5 min	5-30 min	Over 30 min
Neuroendocrine tumors	Up to 5 min	5-30 min	Over 30 min
FUO	Up to 5 min	5-30 min	Over 30 min
Vascular structures in pelvis	Up to 5 min	5-30 min	Over 30 min

EXAMPLE 2

Low Dose Radiopharmaceuticals

The protocols of the present invention are typically performed with low dose radiopharmaceuticals. The following example further describes such doses and provides kits of low dose pharmaceuticals that may be used together with the protocols of the present invention.

The main limitation associated with diagnostic nuclear imaging is the risk associated with humans coming in contact with radioactive materials. In 1901, five years after discovering radioactivity, Henri Becquerel recognized the risks involved in exposure to radioactive isotopes. A short time after he had carried a sample of uranium in his pocket, he observed that the underlying skin developed first erythema (reddening of the skin) and then tissue necrosis, which he attributed to the radioactive properties of the specimen.

Ionizing radiation sources can produce pathological damage by direct cell damage or by producing free radicals which are formed through ionization or excitation reactions and which destruct the chemical integrity of biological molecules such as DNA and proteins, leading to cell death and cancer. Radiation damage to DNA is due primarily to indirect action of radicals, which leads to the lethal and mutagenic effects attributed to ionizing radiation. On the other hand, the same effect is harnessed therapeutically as more rapidly dividing cells are more sensitive to ionizing radiation.

Other than being a source of ionizing radiation, most radioisotopes and radiopharmaceuticals such as heavy metals, and some targeting (recognition binding) moieties of radiotracers are chemically and/or metabolically toxic, and can disrupt enzymatic reactions and other metabolic processes in the body.

The current conservative hypothesis assumes that some risk is associated with even the smallest doses of radiation. Furthermore, it is long known that while there are safety guidelines for exposure to ionizing radiation such as radioactivity, any dose is harmful because radiative damage is cumulative over the life span. Today, after more than a century of careful review of the evidence for radiation effects from the radiation doses associated with diagnostic nuclear medicine, there appears to be little reason for apprehension about either genetic or somatic effects (including thyroid cancer) if exposure is controlled, monitored and utterly minimized. Most practitioners and regulation agencies base their dosage regimes on the Nuclear Regulation Committee (NRC) guidelines and follow NRC regulations.

In order to reduce the harmful effects of radiopharmaceuticals and radiotracers, medical use of these chemicals is closely monitored and controlled by the NRC which has issued strict guidelines for the manufacture, storage and maximal doses administered of such substances (Siegel, J. A., *Guide for Diagnostic Nuclear Medicine*, 2002, U.S. Nuclear Regulatory Commission).

Diagnostic dose guidelines are set according to the effect of the radiopharmaceutical on body tissue. One parameter which is useful in setting dose limits of diagnostic radiopharmaceuticals is the effective dose equivalence (EDE) which can be expressed as Roentgen Equivalent Man (rem, the amount of ionizing radiation required to produce the same biological effect as one rad of high-penetration x-rays) or Sievert (Sv) units, as this unit is defined hereinbelow, wherein 1 rem equals 0.01 Sv.

Following are the acceptable definitions of the units serving to measure radiation doses and effective dose equivalents (EDE, described *supra*).

The Sievert (symbol Sv) or millisievert (mSv) is an SI (International Standards and Units Organization) derived unit of equivalent dose or effective dose of radiation, and so is dependent upon the biological effects of radiation as opposed to the physical aspects, which are characterized by the absorbed dose, measured in grays (see, definition below). The millisievert (mSv) is commonly used to measure the effective dose in diagnostic medical procedures, e.g., X-rays, nuclear medicine, positron emission tomography (PET) and computed tomography (CT). For example, the natural background effective dose rate varies considerably from place to place, but typically is around 3.5 mSv/year. For a full body equivalent dose, 1 Sv causes slight

blood changes, 2-5 Sv causes nausea, hair loss and hemorrhage, and will cause death in many cases. More than 3-6 Sv will lead to death in less than two months in more than 80 % of cases.

The Becquerel (symbol Bq) is the SI derived unit of radioactivity, defined as the activity of a quantity of radioactive material in which one nucleus decays per second. It is therefore equivalent to second^{-1}. The older unit of radioactivity was the curie (Ci), defined as 3.7×10^{10} becquerels or 37 GBq. It was named after Henri Becquerel, who shared a Nobel Prize with Marie Curie for their work in discovering radioactivity. In a fixed mass of radioactive material, the number of becquerels changes with time. In some circumstances, amounts of radioactive material are given after adjustment for some period of time. For example, one might quote a ten-day adjusted figure, that is, the amount of radioactivity that will still be present after ten days. This deemphasizes short-lived isotopes.

The curie (symbol Ci) or millicurie (mCi) is a former unit of radioactivity, defined as 3.7×10^{10} decays per second. This is roughly the activity of 1 gram of the radium isotope ^{226}Ra, a substance studied by the pioneers of radiology, Marie and Pierre Curie. The Ci has been replaced by Bq. One Bq = 2.7027×10^{-11} Ci

The gray (symbol Gy) or milligray (mGy) is the SI unit of energy for the absorbed dose of radiation. One gray is the absorption of one joule of radiation energy by one kilogram of matter. The gray replaced the rad, which was not coherent with the SI system. One Gy equals 100 rads.

Rem (symbol rem) is the amount of ionizing radiation required to produce the same biological effect as one rad of high-penetration x-rays.

Radiation absorbed dose (symbol rad) is a unit of radiation dose or the amount of radiation absorbed per unit mass of material. Rad was superseded in the SI by the Gy. The United States is the only country to still use the rad. Rads are often converted to units of rem by multiplication with quality factors to account for biological damage produced by different forms of radiation. The quality factor for X-rays is 1, so rads and rems are equivalent.

EDE (effective dose equivalence) takes into account the type of radiation, half life and distribution of an isotope to derive a number which represents the effect on human tissues for milliCurie (mCi, as this unit is defined hereinbelow) of the isotope administered.

For example, brain perfusion SPECT imaging performed by administration of a 20 mCi dose of ^{99m}Tc is equivalent to 0.7 rem. This EDE value is similar to that received during a radionuclide bone scan, is 1.5 times that received from a CT of the abdomen and the pelvis, and is 43 % of the annual average background radiation in the United States.

When administered to a 70 kg adult male, the average EDE of such doses falls within a range of 0.5 to 1.5 rem. Table 86 below presents typical doses from several commonly practiced nuclear medicine exams and scans based on a 70 kg individual, and provide information on prior art diagnostic radiopharmaceutical doses utilized to carry out these scans.

Table 86

Nuclear Medical Scan	**Radiopharmaceutical**	**Activity mCi (mBq)**	**Effective Dose mrem (mSv)**
Brain	$^{99m+}$Tc DTPA	20 (740)	650 (6.5)
Brain	^{15}O water	50 (1,850)	170 (1.7)
Brain	^{99m}Tc HMPAO	20 (740)	690 (6.9)
Hepatobiliary	^{99m}Tc SCO	5 (185)	370 (3.7)
Bone	^{99m}Tc MDP	20 (740)	440 (4.4)
Lung Perfusion/Ventilation	^{99m}Tc MAA & ^{133}Xe	5 & 10 (185 & 370)	150 (1.5)
Kidney	^{99m}Tc DTPA	20 (740)	310 (3.1)
Kidney	^{99m}Tc MAG3	20 (740)	520 (5.2)
Tumor	^{67}Ga	3 (110)	1,220 (12.2)
Heart	^{99m}Tc sestimibi	30 (1,100)	890 (8.9)
	^{99m}Tc pertechnetate	30 (1,100)	1,440 (14.4)
Heart	^{201}Tl chloride	2 (74)	1,700 (17)
	^{99m}Tc tetrofosmi	30 (1,100)	845 (8.45)
Various	^{18}F FDG	10 (370)	700 (7.0)

The regulations for use of radiopharmaceuticals changes in cases of patients with lower mass, such as fetuses, infants and children. If a pregnant patient undergoes a diagnostic nuclear medicine procedure, the embryo/fetus will be exposed to radiation. Typical embryo/fetus radiation doses for more than 80 radiopharmaceuticals have been determined by Russell *et al.* (*Health Phys.*, 1997, 73: 756–769). For the most common diagnostic procedures in nuclear medicine, the doses range from 0.5×10^{-4} to 3.8 rad, the highest doses being for ^{67}Ga. Most procedures result in a dose that is a factor of 10 or more lower than the 3.8 rad dose.

In situations involving the administration of radiopharmaceuticals to women who are lactating, the breastfeeding infant or child will be exposed to radiation through intake of radioactivity in the milk, as well as external exposure from close proximity to the mother. Radiation doses from the activity ingested by the infant have been estimated for the most common radiopharmaceuticals used in diagnostic nuclear medicine by Stabin and Breitz (*J. Nucl. Med.*, 2000, 41:862–873). In most cases, no interruption in breast feeding is needed to maintain a radiation dose to the infant well below 100 mrem (1 mSv). Only brief interruption (hours to days) of breast feeding was advised for ^{99m}Tc-macroaggregated albumin, ^{99m}Tc-pertechnetate, ^{99m}Tc-red blood cells, ^{99mTc}-white blood cells, ^{123}I-metaiodobenzylguanidine, and ^{201}Tl. Complete cessation was suggested for ^{67}Ga-citrate, ^{123}I-sodium iodide, and ^{131}I-sodium iodide. The recommendation for ^{123}I was based on a 2.5 % contamination with ^{125}I, which is no longer applicable.

Representative data of radiation dose estimates for a number of radiopharmaceuticals commonly used in nuclear medicine; each listed in a table for all major source organs, several other organs typically of interest, and the effect of an administered dose (per mCi) of a specific radiopharmaceutical on target organs expressed in rem per mCi, is presented in Appendix 1 hereinbelow. Data was collected from "Radiation Dose Estimates for Radiopharmaceuticals" by Michael G. Stabin, James B. Stubbs and Richard E. Toohey of the Radiation Internal Dose Information Center, Oak Ridge Institute for Science and Education, mail stop 51, P.O. Box 117, Oak Ridge, TN 37831-0117.

Although the presently administered doses of radiopharmaceuticals are considered safe, there is a great need to substantially reduce the radiation and toxic

effects attributed to use of such substances.Due to the finite sensitivity exhibited by today's imaging probes, currently established doses of radiopharmaceuticals are at the upper limits of those allowed by the NRC.

One inherent limitation of radioactive-emission imaging stems from the weighing of risks and benefits, namely the conflict between the requirement to limit the use of potentially harmful radioactive isotopes on one hand, and the need to generate sufficient photons from the diagnosed subject in order to produce a meaningful image on a camera or detector of limited sensitivity, on the other. Although low amounts of such radioisotopes are typically administered so as to not exceed recommended doses, currently available detectors require substantial and potentially hazardous amounts of radioisotopes in order to efficiently detect emission. This problem is intensified in cases where a patient is required to undergo several diagnostic procedures over the time of disease treatment, and more so in cases where the patient is a pregnant woman, an infant or a child.

Another limitation of the currently used techniques is the relatively short time periods which are available to the practitioner to collect diagnostic nuclear images due to decay of the radioisotopes (most diagnostic radiopharmaceuticals are characterized by short half-life), and rapid clearance of the diagnostic radiopharmaceuticals from the body by natural bio-processes. Moreover, the rapid decay and clearance of the radiopharmaceuticals prevents sufficient diagnosis of a dynamic system such as the body, wherein a series of images must be taken, so as to characterize a constantly changing environment. In these cases, a static image will not suffice but rather a series of images, much like in a movie. Again, this limitation could have been partially lessened if high dosage could be administered or images could be collected by more sensitive devices.

Thus, although the presently administered doses of diagnostic radiopharmaceuticals are considered safe there is still a widely recognized need for, and it would be highly advantageous to have radiopharmaceutical kits and methods in which the radiation and toxic effects of the radiopharmaceuticals are substantially reduced, whereby the diagnosis quality is at least maintained and desirably improved.

The present inventors have recently devised and constructed single and multi-collector emission detection probes which have vastly improved emission collection capabilities which enable highly sensitive and/or short-termed image capture. These

novel emission detection/collection systems are at least ten-fold more efficient than presently utilized systems (the ratio of measured radiation to emitted radiation is at least 10 to 100-fold higher than prior art systems). This is primarily due to the use of either very sensitive radioactivity emission detectors coupled to high resolution position sensing detectors or to the use of multiple scannable detectors, and further to the use of dedicated algorithms as is disclosed, for example, in the following international applications: PCT/IL2005/000394, PCT/IL2005/000572, PCT/IL2005/000575, PCT/IL2005/000048, WO20040054248 and WO200216965, the contents of which are hereby incorporated by reference. These novel systems employ emission probes which are highly efficient in collecting emissions and thus enable, in combination with dedicated processing algorithms, more sensitive and accurate emission mapping.

The present inventors have now envisioned that the exceptional performance of the abovementioned device, can be efficiently utilized in diagnostic nuclear medicine and imaging, by opening a path to the desired minimization of exposure to ionizing radiation of patients and staff members and/or to the desired high resolution imaging.

The present invention is of diagnostic radiopharmaceutical dose units and methods of using same in diagnostic nuclear imaging. Specifically, the present invention can be used to image specific tissue such as pathological tissue and acquire dynamic imagery while minimizing the harmful effects of radiation caused by use of ionizing radiation sources in diagnostic radiopharmaceuticals. The present invention can further be used to image tissues while utilizing otherwise inefficient radiopharmaceuticals (e.g., having inherent low emission rate) and/or to perform dynamic imagery during short time periods and/or in high resolution.

The principles and operation of the present invention may be better understood with reference to the drawings and accompanying descriptions.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be

understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

The use of radioactive substances which produce ionizing radiation is necessary for advanced methods of pathologic diagnosis and for planning an optimal treatment regime of a growing number of medical conditions. Use of radioactive substances allows the practice of minimally invasive surgical techniques, which save the patients most of the trauma, pain, suffering, hospitalization, recovery and adverse complications associated with conventional "open surgical" procedures. Yet, the use of diagnostic radiopharmaceuticals in diagnostic nuclear medicine is associated with some risk since it exposes the probed subject as well as the medical and technical staff to harmful radiation, and further posses the obligation of expensive and complicated disposal of radioactive materials.

In view of the above, there is a constant need to minimize the exposure of any subject, to ionizing radiation. This can be achieved by minimizing the amount/concentration of the radioactive substance and/or the duration of the exposure to the radioactive substance.

A patient undergoing a nuclear medicine procedure will receive a radiation dose. Under present international guidelines it is assumed that any radiation dose, however small, presents a risk.

An effective dose of a nuclear medicine investigation is typically expressed by units of millisieverts (mSv). The effective dose resulting from an investigation is influenced by the amount of radioactivity administered in megabecquerels (MBq), the physical properties of the diagnostic radiopharmaceutical used (e.g., the type of ionizing radiation, the rate of emission and decay), its distribution in the body (e.g., the accumulation of the emitting agent per tissue) and its rate of clearance from the body. For example, effective doses can range from 0.006 mSv for a 3 MBq for ^{51}Cr-EDTA measurement of glomerular filtration rate (measurement of the kidneys' waste filtration and removal) to 37 mSv for a 150 MBq ^{201}Tl non-specific tumor imaging procedure. The common bone scan with 600 MBq of ^{99m}Tc-MDP has an effective dose of 3 mSv.

As mentioned above, the present inventors have developed a system which employs emission probes that are highly efficient in collecting emissions and thus

enable, in combination with dedicated processing algorithms, more sensitive and accurate emission mapping.

These novel systems have encouraged the present inventors to conceive novel diagnostic kits and diagnosis methods which enable (i) substantially lower diagnostic radiopharmaceutical doses (as compared with the presently used doses); (ii) shorter time of exposure (i.e., collecting the imaging data is a shorter time); (iii) use of radioisotopes that have short half-life and which are typically impractical when the presently known imaging devices are utilized; and (iv) mapping of organs in which rapid substance clearance is observed, and any combination of the foregoing.

Furthermore, the present inventors hypothesized that the heightened sensitivity and overall higher efficiency of the data acquisition device, which allows for the shorter exposure time for diagnostic nuclear imaging, will open the possibility of invasive, minimally invasive and noninvasive time-resolved imagery, or dynamic imagery of biological systems in a living organism.

Thus, the present inventors have now uncovered that the use of such probes facilitates the use of substantially lower amounts of diagnostic radiopharmaceuticals than those presently utilized and thus enables packaging and diagnostic use of novel radiopharmaceutical dose units of substantially lower radioactivity. As is illustrated above, the probe and imaging systems described in previous disclosures of the present inventors enable, for the first time, use of substantially lower doses of various diagnostic radiopharmaceuticals in nuclear imaging.

Thus, according to one aspect of the present invention, there is provided a diagnostic pharmaceutical kit which can be utilized in nuclear imaging techniques. The kit contains a packaged dose unit of a diagnostic radiopharmaceutical having an effective dose equivalence (EDE) of 2.5 millirem (mrem) or less per kg body weight of a subject. This packaged dose is considerably lower than the packaged dose of the prior art, and is in line with the general motivation to reduce to a minimum the exposure of the subject to substances which emit ionizing radiation. Preferably, the EDE of the packaged dose unit of the present invention is 0.01 - 2 millirem per kg body weight of a subject, and more preferably it is 0.01 - 1 millirem per kg body weight of a subject.

Similarly, the diagnostic pharmaceutical kit of the present invention contains a packaged dose unit of a diagnostic radiopharmaceutical having an effective dose

equivalence (EDE) of 150 millirem (mrem) or less, which is a typical whole-body dose for a 70 kg person. Preferably, the EDE of the packaged whole-body dose unit of the present invention is 15 - 100 millirem per 70 kg subject, more preferably 15 - 50 millirem per 70 kg subject.

Compared to a typical whole-body dose of $^{99m+}$Tc DTPA of 650 mrem for a brain scan according to prior art, a whole-body dose of the present invention can be as low as 65 mrem and less; compared to a typical whole-body dose of ^{99m}Tc-Sestimibi of 890 mrem for a heart scan according to prior art, a whole-body dose of the present invention can be as low as 89 mrem and less; and compared to a typical whole-body dose of ^{18}F FDG of 700 mrem for a general somatic scan according to prior art, a whole-body dose of the present invention can be as low as 70 mrem and less.

Alternatively, the dose unit can include an amount of a diagnostic radiopharmaceutical which will result in an amount of detected counts sufficient for imaging when using the abovementioned imaging device having a heightened sensitivity. In nuclear medicine, the dose in mCi of a diagnostic radiopharmaceutical can also be determined according to the sensitivity of the detector utilized, the total time of scan and the total counts needed for imaging (typically about 2- 4 x 10^6 for a scanned region and about 10^5 for a target organ such as the heart). These parameters can be utilized to determine the collection efficiency of prior art emission detection systems. For example, in a ^{99m}Tc heart scan a typical administered dose is 20 - 30 mCi of which about 1.2-1.5 % to 1.5 - 4 % are uptaken by the heart (namely 0.3 mCi - 1.2 mCi, typically 0.5 - 1.0 mCi) and a typical scan is conducted for approximately 10 minutes (600 seconds). Since a single mCi accounts for 3.7 x 10^7 counts per second, the efficiency of a typical detection system calculates to approximately 1.8 photons captured for every 10,000 photons emitted from the organ. Since the present system is at least 10 fold more efficient at photon capturing (e.g., capable of capturing at least 1 photon out of every 1000 photons emitted) a tenth of a diagnostic radiopharmaceutical dose can be utilized for scanning. Thus, for the above described example, a packaged dose unit of 2.5 mCi ^{99m}Tc or less can be utilized for imaging a heart over a period of 10 minutes.

Since the dose reaching the target organ (e.g., the heart) is a fraction of the dose administered, for example, and as stated above, in the case of mapping the cardiac muscle, about 1.5 - 4 % of the dose injected intravenously (20 - 30 mCi)

reaches the heart (0.3 mCi in the heart), mapping a directly injected dose unit of 0.03 mCi or less is possible using the systems developed by the present inventors.

As used herein the phrase "packaged dose unit" refers to a dosage unit (or unit dose) which is packaged in one or more containers such as vials, ampoules or a delivery syringe. Preferably, the dose unit is manufactured and packaged for inhalation or injection (intravenous or subcutaneous) according to FDA regulatory guidelines for human use [Rules and Regulations, *Federal Register* (1999),Vol. 64, No. 94, pp 26657-70].

The dose unit may be ready for administration or may require premixing prior to administration. The latter case is exemplified by a radiotracer preparation which includes an isotope attached to a recognition binding moiety such as an antibody, as is detailed hereinbelow.

A diagnostic radiopharmaceutical can be a compound containing one or more radioisotopes *per se*, or, a radiotracer, in which the compound is bound to a recognition moiety, as follows.

In cases where the organ, tissue or cells to be imaged can be characterized by a known specific and localized (fixed) biochemical moieties, such as a peptide, a protein, a receptor, a membrane, a glycan, a nucleic acid (i.e., RNA and/or DNA) or any combination thereof, the radiopharmaceutical can be designed so as to specifically bind to one or more of these biochemical moieties by way of molecular recognition. This binding is afforded by virtue of one or more recognition moieties which form a part of the radiopharmaceutical. These recognition binding moieties are selected so as to have a high affinity to the specific biochemical moieties characterizing the target organ, tissue or cells to be imaged. This affinity allows for the radiopharmaceutical to concentrate at the target organ, tissue or cells at higher rates than the surrounding organs, tissues or cells, thereby affording an image wherein the target organ, tissue or cells are highlighted by the contrast of radioactive emission.

Radiopharmaceuticals having such binding moieties which act as a vehicle for transporting and delivering the radioactive isotope to a specific target are referred to herein as radiotracers. Therefore, the term “radiotracer”, as used herein, refers to a radiopharmaceutical having one or more recognition binding (targeting) moieties attached thereto.

As used herein, the phrase "recognition binding moiety" or "targeting moiety" refers to a moiety that interacts (binds) with a target recognition site by means of molecular recognition, and include, without limitation, a ligand, an inhibitor, a co-factor, an antibody, a monoclonal antibody, an antibody fragment, an antigen, a hapten, a receptor, a receptor affine peptide, a peptide, a protein, a membrane, a nucleotide and a nucleic acid.

Molecular recognition, also known as "host-guest chemistry", is a phenomenon in which molecules are distinguished accurately from other molecules. Chemically, it indicates that certain molecules abnormally bond with certain molecules and are relatively inert with respect to other molecules found in the same environment. This phenomenon involves the three-dimensional positioning of various sub-molecular functionalities which can form interactions via reciprocal actions such as hydrogen bonds, hydrophobic interactions, ionic interactions, aromatic interactions and/or other non-covalent bond interactions and combination thereof. General examples of molecular recognition include ligand-receptor interactions, enzyme-substrate interactions, antibody-antigen interactions, biotin-avidin affinity interactions and the like.

Non-limiting examples of commonly used radiotracers include ^{99m}Tc-Arcitumomab (CEA-Scan™) which is a monoclonal antibody for imaging colorectal tissues afflicted with colorectal cancer, ^{99m}Tc-sestamibi (Cardiolite™) and ^{99m}Tc-tetrofosmin (Myoview™) for imaging the heart of a subject for myocardial perfusion, ^{111}In-Capromab pendetide (ProstaScint™) which is a monoclonal antibody for imaging prostate tissues afflicted with prostate cancer, ^{99m}Tc-Fanolesomab (NeutroSpec™) which is a monoclonal antibody for imaging inflamed and infectious tissues and ^{90}Y/^{111}In-Zevalin (Ibritumomab Tiuxetan) which is a monoclonal antibody directed against the CD20 antigen, whereby this antigen is found on the surface of normal and malignant B lymphocytes.

Any diagnostic radiopharmaceutical can be utilized in the kit of the present embodiments. In general, the kit of the present embodiments may contain a reduced radiation dose emitted from each radiopharmaceutical, which ranges from 0.1 of the dose of the prior art to 0.01 of the dose of the prior art.

Exemplary radiopharmaceuticals that can be utilized in this context of the present invention include, without limitation, ^{3}H-water, ^{3}H-inulin, ^{11}C-

carbonmonoxide, ^{13}N-ammonia, ^{14}C-inulin, ^{15}O-H_2O, ^{15}O-O_2, ^{18}F-fluorodeoxyglucose, ^{18}F-sodium fluoride, ^{51}Cr-erythrocytes (RBC), ^{57}Co-vitamin B_{12} (cyanocobalamin), ^{58}Co-vitamin B_{12} (cyanocobalamin), ^{59}Fe-citrate, ^{60}Co-vitamin B_{12} (cyanocobalamin), ^{67}Ga-citrate, ^{68}Ga-citrate, ^{75}Se-selenomethionine, ^{81m}Kr-krypton for inhalation, oral administration or injections, ^{82}Rb, ^{85}Sr-nitrate, ^{90}Y/^{111}In-ibritumomab tiuxetan (^{90}Y/^{111}In-Zevalin), ^{99m}Tc-albumin microspheres, ^{99m}Tc-disofenin, lidofenin and mebrofenin, ^{99m}Tc-DMSA, ^{99m}Tc-DTPA (injection), ^{99m}Tc-DTPA (aerosol), ^{99m}Tc-ECD (ethylene cystate dimer), ^{99m}Tc-exametazime (HMPAO), ^{99m}Tc-glucoheptonate, ^{99m}Tc-HEDP, ^{99m}Tc-HMDP, ^{99m}Tc-HSA, ^{99m}Tc-MAA, ^{99m}Tc-MAG_3, ^{99m}Tc-MDP, ^{99m}Tc-tetrofosmin (Myoview), ^{99m}Tc-sestamibi (Cardiolite), ^{99m}Tc-oral administrations, ^{99m}Tc-pertechnetate, ^{99m}Tc-pyrophosphate, ^{99m}Tc-RBC *in vitro* and *in vivo* labeling, ^{99m}Tc-sulfur colloid, ^{99m}Tc-teboroxime, ^{99m}Tc-white blood cells, ^{111}In-ibritumomab tiuxetan (^{111}In-Zevalin), ^{111}In-DTPA, ^{111}In-platelets, ^{111}In-RBC, ^{111}In-white blood cells, ^{123}I-hippuran, ^{123}I-IMP, ^{123}I-mIBG, ^{123}I-sodium iodide, ^{124}I-sodium iodide, ^{125}I-fibrinogen, ^{125}I-IMP, ^{125}I-mIBG, ^{125}I-sodium iodide, ^{126}I-sodium iodide, ^{130}I- sodium iodide, ^{131}I-hippuran, ^{131}I-HSA, ^{131}I-MAA, ^{131}I-mIBG, ^{131}I-Rose Bengal, ^{131}I-sodium iodide, ^{127}Xe-inhalation and injection, ^{133}Xe-inhalation and injection, ^{197}Hg-chlormerodrin, ^{198}Au-colloid and ^{201}Tl-chloride.

Following are several non-limiting examples of the radioactive dose of exemplary radiopharmaceuticals utilized in accordance with this aspect of the present invention. Since an administered dose is typically measured in mCi activity of the radioisotope, the following lists the radioactivity of a packaged dose unit in the kit of the present embodiments, compared to the radioactivity of the presently used doses.

Radioactive ammonia typically comprises a ^{13}N isotope having a half-life of 9.96 minutes. A radioactive dose of ^{13}N-ammonia is typically 20 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{13}N-amminia that ranges from 5 mCi to 0.01 mCi, more preferably from 2 mCi to 0.02 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02 or 0.01 mCi.

Radioactive fluorodeoxyglucose (FDG) typically comprises an ^{18}F isotope having a half-life of 110 minutes. A radioactive dose of ^{18}F-FDG is typically 10 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical

kit comprises a radioactive dose of ^{18}F-FDG that ranges from 3 mCi to 0.1 mCi, more preferably from 1 mCi to 0.1 mCi and thus can be, for example, 3, 1 or 0.1 mCi.

Radioactive capromab pendetide (ProstaScint), typically comprises an ^{111}In isotope having a half-life of 72 hours. A radioactive dose of ^{111}In-capromab pendetide is typically 5 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{111}In-capromab pendetide that ranges from 2 mCi to 0.01 mCi, more preferably from 0.5 mCi to 0.01 mCi and thus can be, for example, 2, 1, 0.5, 0.1, 0.05 or 0.01 mCi.

Radioactive WBCs (non-protein peptide), typically comprises an ^{111}In isotope. A radioactive dose of ^{111}In-WBCs is typically 0.5 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{111}In-WBCs that ranges from 0.2 mCi to 0.001 mCi, more preferably from 0.05 mCi to 0.001 mCi and thus can be, for example, 0.2, 0.1, 0.05, 0.01, 0.005 or 0.001 mCi.

Radioactive Satumomab Pendetide (OncoScint), typically comprises an ^{111}In isotope. A radioactive dose of ^{111}In-Satumomab Pendetide is typically 5 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{111}In- Satumomab Pendetide that ranges from 2 mCi to 0. 01 mCi, more preferably from 0.2 mCi to 0.01 mCi and thus can be, for example, 2, 1, 0.5, 0.1, 0.05 or 0.01 mCi.

Radioactive Pentetreotide typically comprises an ^{111}In isotope. A radioactive dose of ^{111}In-Pentetreotide is typically 6 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{111}In-Pentetreotide that ranges from 1 mCi to 0.005 mCi, more preferably from 0.5 mCi to 0.005 mCi and thus can be, for example, 1, 0.5, 0.2, 0.1, 0.05, 0.01 or 0.005 mCi.

Radioactive Arcitumomab typically comprises a ^{99m}Tc isotope having a half-life of 6 hours. A radioactive dose of ^{99m}Tc- Arcitumomab typically ranges from 20 mCi to 30 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{99m}Tc- Arcitumomab that ranges from 5 mCi to 0.05 mCi, more preferably from 3 mCi to 0.05 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.1 or 0.05 mCi.

Radioactive Sodium pertechnetate typically comprises a ^{99m}Tc isotope. A radioactive dose of ^{99m}Tc-Sodium pertechnetate typically ranges from 10 mCi for a whole-body scan to 0.1 mCi, whereby the packaged dose unit is typically formulated as a drop for an eye scan. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{99m}Tc-Sodium pertechnetate that ranges from 5 mCi to 0.01 mCi, more preferably from 1 mCi to 0.01 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02 or 0.01mCi.

A radioactive dose of Erythrocytes (RBC) comprising a ^{99m}Tc isotope typically ranges from 10 mCi to 25 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{99m}Tc-RBC that ranges from 5 mCi to 0.05 mCi, more preferably from 1 mCi to 0.05 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.1, 0.05, 0.02 or 0.01 mCi.

Radioactive Depreotide (NeoTect), apcitide (AcuTect), pyrophosphate, medronate (MDP), exametazime (HMPAO) and bicisate (ECD, Neurolite) all comprise a ^{99m}Tc isotope. A radioactive does of these radiopharmaceuticals is typically 20 mCi. According to a preferred embodiment of the present invention, radiopharmaceutical kits comprise a radioactive dose of such a ^{99m}Tc-radiopharmaceuticals that ranges from 5 mCi to 0.05 mCi, more preferably from 1 mCi to 0.05 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.2, 0.1, 0.05 mCi.

A radioactive dose of ^{99m}Tc-Sestamibi typically ranges from 10 mCi (for stress) to 30 mCi (for rest). According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of such a ^{99m}Tc-radiopharmaceutical that ranges from 5 mCi to 0.01 mCi, more preferably from 1 mCi to 0.01 mCi and thus can be, for example, 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02 or, 0.01 mCi.

Radioactive Cyanocobalamin typically comprises an ^{57}Co isotope having a half-life of 271.8 days. A radioactive dose of ^{57}Co- Cyanocobalamin is typically 0.001 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{57}Co- Cyanocobalamin that ranges from 0.0003 mCi to 0.00001 mCi, more preferably from 0.0001 mCi to 0.00001 mCi and thus can be, for example, 0.0003, 0.0001, 0.00005 or 0.00001 mCi.

Radioactive Gallium Citrate, typically comprises a ^{67}Ga isotope having a half-life of 271.8 days. A radioactive dose of ^{67}Ga-Gallium citrate is typically 5 mCi for

PET imaging and 10 mCi for SPEC imaging. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{67}Ga-Gallium citrate that ranges from 1 mCi to 0.01 mCi, more preferably from 0.5 mCi to 0.01 mCi and thus can be, for example, 1, 0.5, 0.2, 0.1, 0.05 or 0.01 mCi.

^{81}Kr isotope, having a half-life of 210,000 years, is presently used as a gas for dynamic imaging. A radioactive dose of ^{81}Kr is typically 10 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{81}Kr that ranges from 2 mCi to 0.05 mCi, more preferably from 1 mCi to 0.05 mCi and thus can be, for example, 2, 1, 0.5, 0.1 or 0.05 mCi.

Radioactive sodium iodide typically comprises an ^{123}I isotope having a half-life of 13.2 hours. A radioactive dose of ^{123}I-sodium iodide typically ranges from 0.1 mCi to 0.4 mCi, and the radiopharmaceutical dose unit is often provided in capsules. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{123}I-sodium iodide that ranges from 0.05 mCi to 0.001 mCi, more preferably from 0.01 mCi to 0.001 mCi and thus can be, for example, 0.1, 0.05, 0.02, 0.01, 0.005 or 0.001 mCi, whereby the ^{123}I-sodium iodide can be packaged as capsules.

Radioactive Sodium iodide can alternatively comprise an ^{131}I isotope having a half-life of 8 days. A radioactive does of ^{131}I-sodium iodide typically ranges from 0.01 mCi to 0.004 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{131}I-sodium iodide that ranges from 0.001 mCi to 0.00005 mCi, and thus can be, for example, 0.001, 0.0005, 0.0002, 0.0001 or 0.00005 mCi, whereby the ^{131}I-sodium iodide can be packaged as capsules.

Radioactive albumin typically comprises an ^{125}I isotope having a half-life of 59.4 days. A radioactive does of ^{125}I-albumin is typically 0.02 mCi. According to a preferred embodiment of the present invention, a radiopharmaceutical kit comprises a radioactive dose of ^{125}I-albumin that ranges from 0.005 mCi to 0.0001 mCi, more preferably from 0.001 mCi to 0.0001 mCi and thus can be, for example, 0.005, 0.002, 0.001, 0.0005 or 0.0001 mCi.

Radioactive sodium chromate typically comprises a ^{51}Cr isotope having a half-life of 27.7 days. A radioactive dose of ^{51}Cr-sodium chromate typically ranges from 0.15 mCi to 0.3 mCi. According to a preferred embodiment of the present invention,

a radiopharmaceutical kit comprises a radioactive dose of ^{51}Cr-sodium chromate that ranges from 0.05 mCi to 0.001 mCi, more preferably from 0.01 mCi to 0.001 mCi and thus can be, for example, 0.05, 0.02, 0.01, 0.005 or 0.001 mCi.

As is provided in the list above, the mCi dose range of the present dose unit of each listed exemplary diagnostic radiopharmaceutical is substantially lower than that of prior art dose units.

The kit of the present embodiments can be used with any suitable nuclear imaging technique.

The radiopharmaceutical of the diagnostic kit of the present embodiments can be prepared using any suitable prior art approach. Such approaches are well known to the ordinary skilled artisan and as such no further description of specific synthesis approaches of diagnostic radiopharmaceuticals and in particular radiotracers are provided herein.

However, in cases where the radiopharmaceutical is a radiotracer, it is sometimes preferred that the isotope be provided separate from the recognition binding moiety especially in cases of isotopes exhibiting a short half life, since a specific activity of such a radiotracer preparation will substantially decrease over a short time period.

As mentioned hereinabove, an effective dose of any given radiopharmaceutical is influenced, among other factors, by the amount of the radioisotope and the state of decay of the radioisotope, namely the radioactivity which is currently measured at any given time. In essence, an isotope which already decayed no longer contributes to the activity of the administered sample, and therefore is considered an impurity. In addition, radiopharmaceuticals which contain chelators or recognition moieties attached thereto may decompose, both *in vivo* and *in vitro*, so as to produce, for example, the radioisotope, the chelating moiety and/or the recognition moiety. The free chelators and recognition moieties are also considered impurities.

Radioisotopes utilized for synthesis are therefore typically > 60 % pure, and preferably are > 90 % pure; during radiotracer synthesis, a recognition binding moiety is mixed with a radioisotope and quality is checked to maintain approximately a 95 % pure composition of the radiotracer. The remaining 5 % is composed of non-radioactive isotopes, chelators, recognition moieties and the like.

Following mixing and prior to injection, isotope decay and chemical

decomposition may reduce the specific activity of the diagnostic radiopharmaceutical in proportion to isotope decay time and the instability of the radiopharmaceutical.

Few diagnostic radiopharmaceuticals depend on "specific activity" or purity, since they "compete" for receptors with their decomposition products or their decomposition products produce adverse effects (e.g. to lungs).

The kit of the present invention can further include instructions for use in carrying out a nuclear scan as well as instructions for handling and additional packaging materials (e.g. pig) as required by federal regulations. Radioisotopes must be carefully handled, therefore vials or syringes containing such substances are delivered inside containers offering some degree of radiation shielding. Furthermore, government regulations require syringes to be disposed of in a disposal container that shields others from the risk of injury posed by their sharp, biologically-contaminated hypodermic needles. Such a container generally referred to herein as a "sharps" container, typically has an inner cavity or chamber that can hold one or more syringes.

One type of conventional delivery container currently used for the delivery of syringes containing radioactive drugs is known as a radiopharmaceutical pig. The radiopharmaceutical pig has a shielded inner chamber suitable for enclosing a syringe that is itself held inside of a sharps container. In particular, the chamber is lined with elemental lead to shield individuals from the radioactive drug in the syringe. The exterior of the radiopharmaceutical pig is a plastic polystyrene shell. The sharps container has an insert and a cap that can be engaged by two snaps that fit into two aligned slots formed on the insert.

Prior to administration, the syringe is loaded with the required dose of a radioactive drug and is placed in the insert, which is nested in the chamber of the radiopharmaceutical pig. The radiopharmaceutical pig is then closed and delivered to the hospital, whereupon the pig is disassembled and the syringe is used to inject the dose into the patient. The spent syringe may then be placed back into the sharps insert and the cap may then be placed on the housing to hold the spent syringe within the sharps container. The radiopharmaceutical pig is reassembled and taken to a disposal area, which may or may not be at the pharmacy.

While exposure to ionizing radiation presents a major, widely recognized limit to the presently known nuclear imaging techniques, these techniques are oftentimes limited by other factors. These include, for example, rapid decay of the radioisotope

(i.e., short half-life), rapid clearance of the radiopharmaceutical from the targeted organ, and low energy and/or rate of disintegration of the radiopharmaceutical.

These characteristics determine the amount and energy of detectable photons which reach the detector per time unit. When used with the presently known emission detectors, low amount and/or energy of the detectable photons results in a weak or no signal and hence fail to provide a meaningful image. Thus, for example, radioisotopes that rapidly decay or are rapidly cleared from the target organ, fail to produce a sufficient amount of detectable photons at the time of data collection.

According to the present invention, the highly sensitive emission detector designed by the present inventors can be used to detect sufficient photons from such radioisotopes due to its higher efficiency and wider dynamic range, even for radioisotope characterized by a short half-life, low rate and low energy of disintegration, which may or may not be combined with a low rate of accumulation in the organ of interest and a rapid clearance from the body by metabolic and chemical processes.

The present inventors have now uncovered that the high sensitivity of the novel imaging probes described above can be used, due to higher efficiency and wider dynamic range, to collect sufficient imaging data even in cases of radiopharmaceuticals that are characterized by low amount and/or energy of the emitted photons within a time frame of a nuclear investigation. Thus, these highly sensitive probes enable to perform efficient imagery even with such radiopharmaceuticals that are incompatible or at least inefficient when utilized with the presently known techniques. These radiopharmaceuticals are collectively referred to herein as having an inherent low emission rate, as this phrase is defined hereinbelow.

Each of the radiopharmaceutical kits described herein can be efficiently utilized for obtaining nuclear images of tissue and organs of interest, by employing non- or minimally invasive techniques *in vivo*.

Thus, according to an additional the present invention there is provided a method of imaging a tissue of a subject. The method is effected by administering to the subject, either systemically or locally, a dose unit of a diagnostic radiopharmaceutical having a dose equivalent of 2.5 mrem or less per kg body weight, as detailed hereinabove; collecting the emission produced by the diagnostic

radiopharmaceutical, as detailed hereinbelow; and translating the emission data collected into a two-dimensional or three-dimensional image data.

Typically, the radiopharmaceutical is administered systematically in order to achieve two main goals, a) reach the target organ which is typically out of reach when using noninvasive or minimally invasive techniques, and b) in order to create the appropriate background for the organ to be imaged and obtain the contrast between the areas of interest (those serving as targets for the radiopharmaceutical) and their surrounding. Systematic administration can be effected, for example, by intravenous injection, by inhalation or orally.

As the use of the abovementioned high sensitivity emission detector becomes available, the limitations associated with low signal are alleviated considerably. Thus, imaging of tissues or organs using radiopharmaceuticals that have low emission rate and hence presently lead to collection of insufficient data during a scan, is facilitated.

Thus, according to another aspect of the present invention, there is provided another method of imaging a tissue of a subject. The method, according to this aspect of the present invention is effected by administering to the subject, either systemically or locally, a dose unit of a radiopharmaceutical which is characterized by an inherent low emission rate, as detailed hereinabove; collecting the emission produced by the diagnostic radiopharmaceutical; and translating the emission data collected into a two-dimensional or three-dimensional image data.

The method, according to this aspect of the present invention, therefore allows to use radiopharmaceuticals and to image organs and/or tissues that are otherwise impractical.

The high sensitivity of the emission detector taught by the present inventors further enables to collect sufficient image data in a short time period. This feature is exceptionally advantageous since it allows to minimize the time during which a subject is exposed to radiation. Hence, using any diagnostic radiopharmaceuticals, including the radiopharmaceuticals described herein, nuclear imaging can be performed during a shorter time period, compared to the presently known imaging methods.

Thus, according to a further aspect of the present invention there is provided a method of imaging a tissue, which is effected by administering to the subject a dose unit of a diagnostic radiopharmaceutical; collecting emission of the diagnostic

radiopharmaceutical during a time period that does not exceed, e.g., 1-30 minutes; and translating the emission collected into image data.

The method according to this aspect of the present invention is particularly advantageous in PET and SPECT imaging techniques.

Positron Emission Tomography (PET), is a nuclear medicine imagine technology which requires the administration to a subject of a molecule labeled with a positron-emitting nuclide. Single Photon Emission Computed Tomography (SPECT) is a form of chemical imaging in which emissions from radioactive compounds, labeled with gamma-emitting radionuclides, are used to create cross-sectional images of radioactivity distribution *in vivo*.

These techniques require relatively high emission levels for obtaining a meaningful image. In addition, radiopharmaceuticals that are suitable for use in these techniques are often characterized by relatively short half-lives. Thus, for example, ^{15}O, ^{13}N, ^{11}C and ^{18}F, which are often used in PET, have half-lives of 2, 10, 20, and 110 minutes, respectively. Due to the high emission level required and the short half-lives of the radiopharmaceuticals, relatively high radiation doses of the radiopharmaceuticalre administered to the subject.

Performing such nuclear imaging procedures in relatively short time periods is therefore exceptionally beneficial since it reduces the time the subject is exposed to high radiation level.

The ability to obtain all the required data during a short time period, which is not possible with other currently used detectors, further allows the investigator to collect several consecutive images during that time scan in which the emission rate is still sufficient for significant data collection.

These consecutive images can be used to provide time-resolved data of the tissue or organ of interest, showing the development in time of imaged system.

Thus, according to preferred embodiments of the present invention, for any of the methods described herein, a time-resolved data can be obtained by performing consecutive images of the investigated tissue.

Nuclear imaging techniques suffer from other limitations which are related to a weak signal or a low signal-to-noise ratio. Such limitations stem from the fact that any detector has a limited sensitivity, and at any dose of the radiopharmaceutical, only

a fraction of the emitted radiation can be picked-up by the detector and/or be distinguished from the background noise.

Using the improved emission detector taught by the present invention can further enable and facilitate the provision of a high-resolution image of a tissue, which so far was impossible, difficult or required exceptionally high doses of the radiopharmaceuticalnd/or prolonged exposure of the subject to the radiopharmaceutical t.

Thus, according to an aspect of the present invention, there is provided a method of obtaining a high-resolution image of a tissue of a subject.

Any suitable extracorporeal or intracorporeal imaging technique employing any suitable probe types can be used to image the administered diagnostic radiopharmaceutical in the methods described herein. Preferably an imaging system employing a probe having a wide angle or a wide view of collection is employed.

Further preferably, the emission data is collected by one or more radioactive-emission probes which are characterized by a collection efficiency of 1 %, each of which is separately adjustable within its housing.

Further preferably, the radioactive-emission probes, or emission detectors are scintillation probes which have a collection angle that enables a collection target area of 15 mm^2 when placed 15 cm away from the target area.

Extra and intra-corporeal probe types which are highly suitable for use with the kit of the present invention are described in detail in the PCT applications referenced hereinabove.

A non-limiting example of a widely used radiopharmaceutical, ^{99m}Tc-sastamibi, is used herein to demonstrate the various novel features of the present invention. ^{99m}Tc is characterized by a half-life ($t_{½}$) of 6.02 hours. Table 86a below presents the physical decay of ^{99m}Tc, wherein the calibration time is set to 0 arbitrarily and the activity is defined as 100 %. The remaining fraction of radioactivity is recorded every hour from that time point. This decay chart is used by the medical staff when preparing the sample for injection into a patient undergoing diagnostic imaging. The absolute activity of the product is measured at the manufacturer site on the day of shipment, and the complete assay data is provided on the tag attached to the vial.

Table 86a

Hours	Fraction remaining
0	1.000 (100 %)
1	0.891 (89.1 %)
2	0.794 (79.4 %)
3	0.708 (70.8 %)
4	0.631 (63.1 %)
5	0.562 (56.2 %)
6	0.501 (50.1 %)
7	0.447 (44.7 %)
8	0.398 (39.8 %)
9	0.355 (35.5 %)
10	0.316 (31.6 %)
11	0.282 (28.2 %)
12	0.251 (25.1 %)

Apart for radioactivity decay, the product is cleared from the body by natural processes. Myocardial uptake which is coronary flow dependent is 1.2 % of the injected dose at rest and 1.5 % of the injected dose at exercise. Table 87 below illustrates the biological clearance as well as effective clearance which include biological clearance and radionuclide decay of ^{99m}Tc-Sestamibi from the heart and liver.

Table 87

	Rest				Stress			
Time	Heart		Liver		Heart		Liver	
(minutes)	Biological	Effective	Biological	Effective	Biological	Effective	Biological	Effecti
5	1.2	1.2	19.6	19.4	1.5	1.5	5.9	5.8
30	1.1	1.0	12.2	11.5	1.4	1.3	4.5	4.2

60	1.0	0.9	5.6	5.0	1.4	1.2	2.4	2.1
120	1.0	0.8	2.2	1.7	1.2	1.0	0.9	0.7
240	0.8	0.5	0.7	0.4	1.0	0.6	0.3	0.2

The agent is excreted without any evidence of metabolism. The major pathway for clearance of ^{99m}Tc-Sestamibi is the hepatobiliary system. Activity from the gall bladder appears in the intestines within one hour of injection. Twenty-seven percent of the injected dose is excreted in the urine, and approximately thirty-three percent of the injected dose is cleared through the feces in 48 hours.

A typical published preparation procedure of ^{99m}Tc-Sestamibi [CARDIOLITE®, *Kit for the Preparation of Technetium Tc99m Sestamibi for Injection*, Document No. 513121-0300, March 2000, DuPont Pharmaceuticals Company, Billerica, Massachusetts, USA] includes transferring a known volume of a solution containing the radioactive isotope sodium salt into a vial containing the rest of the ingredients, including the MIBI (2-methoxy isobutyl isonitrile) component. This amount should correspond to 925-5550 MBq (25-150 mCi) in approximately 1 to 3 ml. After heating the reaction mixture, the reaction vial sample is assayed using a suitable radioactivity calibration system, and the results of the assay determine the amount which will be injected into the patient. According to this prior art procedure, the prepared product should be stored at 15-25 °C before and after reconstitution and used within 6 hours after preparation. The patient dose and radiochemical purity (see the abovementioned Document No. 513121-0300 for procedures) should be measured by a suitable radioactivity calibration system immediately prior to patient administration.

As can be deduced from the above description, there are two major physical attributes which determine the time regime for the nuclear imaging process which are crucial for its effectiveness: the rate of decay and the rate of clearance.

According to the present invention, the above procedure can be altered in two principle ways; one addresses the decay chronology and the other addresses the quantity required for effective imaging of the relevant organ in the patient. Since the sensitivity of the emission detector associated with the present invention is 10-100 folds higher than the currently used detectors, a kit according to the present invention

may contain a smaller amount of the radioactive isotope to be used, or may allow a longer time for data collection after administration, as compared to the presently known kits. The latter allows for data collection of dynamic processes which take place in the patient, i.e., following in-vivo changes in the organs which are monitored by the nuclear imaging technique, hence allowing for time-resolved analysis of the medical condition of interest.

Other examples for the preparation procedure of any commercially available radiopharmaceuticalnd radiotracer can be in the instruction documents provided in presently available kits, such as the kit for the preparation of ^{111}Indium Capromab Pendetide. ^{111}Indium Capromab Pendetide is a radiotracer containing a murine monoclonal antibody, 7E11-C5.3 (the site-specific delivery vehicle), which is covalently conjugated to the linker-chelator, glycyl-tyrosyl-(N,-diethylenetriaminepentaacetic acid)-lysine hydrochloride (GYK-DTPA-HCl). The 7E11-C5.3 antibody is of the IgG1, kappa subclass (IgG1K). This antibody is directed against a glycoprotein expressed by prostate epithelium known as prostate specific membrane antigen (PSMA). The PSMA epitope recognized by monoclonal antibody (MAb) 7E11-C5.3 is located in the cytoplasmic domain. The radioisotope ^{111}In is brought in contact with the antibody-linker-chelator conjugate upon preparation of the sample prior to administration, and the indium is therefore incorporated into the site-specific delivery vehicle. Detailed quantities, characteristics and procedures for the preparation of this radiotracer for administration can be found in http://www.cytogen.com/professional/prostascint/pi.php.

As in the example of ^{99m}Tc-sestamibi, ^{111}Indium capromab pendetide (ProstaScint®) is provided as a two-vials kit which contain all of the non-radioactive ingredients necessary to produce a single unit dose of ^{111}In ProstaScint®, an immunoscintigraphic agent for administration by intravenous injection only. The ProstaScint® vial contains 0.5 mg of capromab pendetide in 1 ml of sodium phosphate buffered saline solution adjusted to pH 6; a sterile, pyrogen-free, clear, colorless solution. The vial of sodium acetate buffer contains 82 mg of sodium acetate in 2 ml of water for injection adjusted to pH 5-7 with glacial acetic acid; it is a sterile, pyrogen-free, clear, and colorless solution. The sodium acetate solution must be added to the sterile, non-pyrogenic high purity ^{111}InCl solution to buffer it prior to

radiolabeling ProstaScint®. The immunoscintigraphic agent ^{111}In capromab pendetide is formed after radiolabeling with ^{111}In.

Use of novel low doses of Radiopharmaceuticals, typically Radiopharmaceuticals which result in less than 2.5 mrem EDE per Kg body weight (e.g., less than 2 mCi of Tc-99m) is enabled through the use of more sensitive emission detectors such as those described in PCT/IL2005/000394, PCT/IL2005/000572, PCT/IL2005/000575, PCT/IL2005/000394 and PCT/IL2005/000048, hereby included in their entirety by reference.

Table 88 below provides typical prior art doses and novel low doses of radiopharmaceuticals that are effectively imaged using the emission detection systems described in the above referenced PCT applications.

Table 88

Radiopharmaceutical		Typical Purity in %	Prior art dose in mCi (range)	Dose utilized by present invention mCi (range)
Positron Emission Isotopes				
ISOTOPE/Half-Life Time				
Ammonia N 13	9.96 min		20	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.01
Fludeoxyglucose F-18	110 min		10	0.1-3 preferably - 3, 1, 0.1
Sodium Fluoride F-18	110 min			0.1-3 preferably - 3, 1, 0.1
Methionine C-11	20.4 min			

O-15	2.04 min
Rubidium Rb-82	1.27 min
Cu-62	9.8 min
Ga-68	68.1 min

Protein/peptide/antibody + Isotopes

Indium-111 Capromab pendetide (ProstaScint)	>90% (inject after up to 8 hours from mixing, isotope 1/2L ~72hr)	5	0.01-2 Preferably - 2, 1, 0.5, 0.1, 0.05, 0.01
Indium In-111 WBCs (non-protein,peptide)		0.5	0.001-0.2 Preferably - 0.2, 0.1, 0.05, 0.01, 0.005, 0.001
Indium In-111 Satumomab Pendetide (OncoScint)		5	0.01-2 Preferably - 2, 1, 0.5, 0.1, 0.05, 0.01
Technetium Tc 99m Arcitumomab (CEA-Scan)	>60% (shelf life up to 4hr / 6hr half-life)	20-30	0.05-5 Preferably - 5, 2, 1, 0.5, 0.1, 0.05
Technetium Tc 99m Fanolesomab (Neutrospec)		75-25mcg of Fanolesomab is labeled with10-20mCi	
Technetium Tc 99m Nofetumomab			

Merpentan†		
Non-peptide/protein based isotopes		
Cyanocobalamin Co 57	0.001	0.00001-0.0003 Preferably - 0.0003, 0.0001, 0.00005, 0.00001
Ferrous Citrate Fe 59		
Gallium Citrate Ga 67	5 10 for SPECT	0.01-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01
Indium In 111 Oxyquinoline		
Indium In 111 Pentetate		
Indium In 111 Pentetreotide	6	0.005-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005
Iobenguane, Radioiodinated		
Iodohippurate Sodium I 123		
Iodohippurate Sodium I 131		
IofetamineI 123		
Iothalamate Sodium I 125		
Krypton Kr 81m	10 (as a gas,	0.05-2

		USED FOR DYNAMIC IMAGING)	Preferably - 2, 1, 0.5, 0.1, 0.05
Iodide 125 Albumin		0.02	0.0001-0.005 Preferably - 0.005, 0.002, 0.001, 0.0005, 0.0001
Radioiodinated Albumin			
SodiumChromate Cr 51		0.15 0.1-0.3	0.001-0.05 Preferably - 0.05, 0.02, 0.01, 0.005, 0.001
Sodium Iodide I 123		0.4, (also 0.1-0.2 as capsules)	0.001-0.05 Preferably - 0.1, 0.05, 0.02, 0.01, 0.005, 0.001 Also as capsules
Sodium Iodide I 131		0.004-0.01	0.00005-0.001 Preferably - 0.001, 0.0005, 0.0002, 0.0001, 0.00005
(Sodium) Pertechnetate Tc 99m		10 100-200 micro for eye imaging (1 drop per eye) 1mCi for cyctogram	0.01-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.01
Technetium Tc 99m Albumin			
Technetium Tc 99m Albumin Aggregated	NO LESS THAN 90% AT PREPARATION	1-4 2mCi in each leg	0.001-0.5 Preferably - 0.5, 0.2, 0.1, 0.05, 0.02,

	(Up to 6 additional hours on the shelf turns it into 45%), AS BEYOND A LEVEL IT MAY BLOCK LUNGS CAPILLARY – USED TO DETECT PULMONARY EMBOLISM DUE TO DVT		0.01, 0.005, 0.002, 0.001
Technetium Tc 99m Albumin Colloid			
Technetium Tc 99m Erythrocytes (RBCs)		10-20 20-25 for liver perfusion & SPECT	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.01
Technetium Tc 99m Depreotide (NeoTect)		20	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05
Technetium Tc 99m Apcitide (AcuTect)		20	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05
TechnetiumTc 99m Bicisate (ECD, Neurolite)		20	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05
Technetium Tc 99m DMSA Dimercaptosuccinic acid (Succimer)		2-6 (typically 5)	0.005-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005
Technetium Tc 99m Disofenin		5	0.005-1

(HIDA)		Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005
TechnetiumTc 99m Exametazime (HMPAO)	20	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05
Technetium Tc 99m Gluceptate		
TechnetiumTc 99m Lidofenin		
Technetium Tc 99m Mebrofenin	5mCi (non-jaundiced)8mCi (jaundiced)	
TechnetiumTc 99m Medronate (MDP)	20 15	0.05-5 Preferably - 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.01
Technetium Tc 99m Mertiatide (MAG3)	5-10	0.005-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005
Chromic Phosphate	4	0.05-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01
SR 89 Chloride (Metastron)	4 (this is for palliative treatment)	0.05-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.01
Technetium Tc 99m Oxidronate		
Technetium Tc 99m Pentetate	3-5 (for GFR), 10-	3 (brain/renal

(DTPA)	20 (for brain, renal perfusion)	perferred) 0.005-1 Preferably - 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.01, 0.005
TechnetiumTc 99m Pyrophosphate	15 20 for muscle necrosis	0.005-5 Preferably - 5, 2, 1, 0.5, 0.3, 0.1, 0.05, 0.02, 0.01, 0.005
Technetium Tc 99m (Pyro- and trimeta-) Phosphates		
Technetium Tc 99m Sestamibi (Cardiolite, Miraluma – for breast imaging)	10-30 (typically 10 for rest and 30 for stress)	0.01-5 preferably 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.01
Technetium Tc 99m Sulfur Colloid		
Technetium Tc 99m Teboroxime		
Technetium Tc 99m Tetrofosmin (MyoView)	5-33 (typical 8-20)	
Technetium Tc 99m HDP	20-25 < 30 years 25-30.30yrs & obese	
Technetium Tc 99m Sulpher colloid	12mCi/70kg	
Thallous Chloride Tl 201	0.055 mCi/kg	
Xenon Xe 127	5-10	
Xenon Xe 133	5-10	

Use of radiopharmaceutical cocktails yields generations of new products (premixed radiopharmaceutical pairs) and diagnostic procedures that enable multi-dimensional, differential diagnosis and use of one diagnostic procedure for revealing any pathology. Radiopharmaceutical cocktails also require significantly lower radiopharmaceutical dosage and results in several-fold increase in sensitivity as well as a 90% procedure time reduction and significant improvement in spatial and spectral resolution.

Radiopharmaceutical combinations are exemplified in a liver-spleen scan using +RBC +gallium (for cases of liver SOL/hemangioma/abscess/hepatoma). Bone scan +gallium or bone scan +In-WBC (for osteomyelitis). Perfusion rest/stress+MIBG for autonomic system in heart, mapping+BMIPP for heart failure with the addition of FDG for viability.

Assessment of the sentinel lymph node of tumors via Lymphoscintigraphy, (melanoma, breast, etc) with addition of FDG (and optionally MIBI) to assess the presence of tumor in these nodes (typically effected by peri-tumoral injection for lymphoscintigraphy and IV FDG). Although low doses are preferred for the reasons set forth hereinabove, higher doses can also be utilized in combinations provided one can effectively isolate the signal resultant from each radiopharmaceutical.

EXAMPLE 4

Unified management of radiopharmaceutical dispensing, administration, and imaging

Methods and kits of the present invention may be administered and imaging followed using the following exemplary end-to-end automated system.

Figure 100 is a schematic illustration of an end-to-end automated system 10a for medical imaging, in accordance with an embodiment of the present invention. System 10a comprises a plurality of integrated elements that are configured to electronically exchange information among one another. The elements include an automated radiopharmaceutical dispensing system 20a, a portable information-bearing radiopharmaceutical agent container 22a, a portable patient-specific data carrier 24a, an automated administration system 26a, and an automated imaging system 28a. The systems perform their respective automated functions at least in part responsively to the exchanged information. The elements typically authenticate one another via the

exchanged information, in order to ensure that only authorized elements participate in the system, and that only authorized and appropriate functions are performed. Each of the elements is described in detail hereinbelow.

An end-to-end system of the present invention may comprise a plurality of integrated elements that are configured to electronically exchange information among one another. The elements include an automated radiopharmaceutical dispensing system, a portable information-bearing radiopharmaceutical agent container, a patient management system, a portable patient-specific data carrier, an automated administration system, and an automated imaging system. The systems perform their respective automated functions at least in part responsively to the exchanged information. The elements typically authenticate one another via the exchanged information, in order to ensure that only authorized elements participate in the system, and that the systems perform only authorized and appropriate functions.

The exchanged information typically includes patient-specific data, radiopharmaceutical agent-specific data, and/or patient- or radiopharmaceutical agent-specific imaging protocol data. Such data enable the systems to customize their respective automated functions for specific patients, radiopharmaceutical agents, indications, and/or imaging procedures. For some applications, the exchanged information includes commercial license information relating to the use of a specific protocol with a specific radiopharmaceutical agent, and one or more of the systems are configured to verify the license information before performing their respective functions.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container and/or the patient-specific data carrier is configured to contain protocol information for performing an imaging procedure using the labeled radiopharmaceutical agent (also referred to herein and in the claims as "radiopharmaceutical") held by the container. For some applications, the protocol information includes SPECT imaging protocol information, and the imaging system uses the protocol information to perform a SPECT imaging procedure using the labeled radiopharmaceutical agent contained in the container. For some applications, the agent container contains a single dose of the labeled radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container or the patient-specific data carrier is configured to contain at least one kinetic parameter of the labeled radiopharmaceutical agent contained in the container. The imaging system uses the kinetic parameter to perform a dynamic SPECT imaging procedure.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container contains radiopharmaceutical information regarding the labeled radiopharmaceutical agent contained in the container. The portable patient-specific data carrier is configured to contain patient information regarding the patient, and imaging protocol information for use with the labeled radiopharmaceutical agent, such as SPECT imaging protocol information. The imaging system uses the protocol information to perform an imaging procedure, such as a dynamic SPECT imaging procedure. For some applications, the patient-specific data carrier comprises a coupling mechanism configured to be coupled to the patient. For example, the coupling mechanism may comprise a bracelet, a watch, a necklace, or another wearable article.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container contains a first identifier value, and the patient-specific data carrier contains a second identifier value. The imaging system is configured to perform an imaging procedure responsively to a detection of a correspondence between the first and second identifier values. For some applications, the first identifier value equals the second identifier value, while for other applications the values do not equal one another, but instead correspond to one another based on information provided by an element of the end-to-end system. For some applications, the first and/or second identifier values are arbitrarily assigned, or pre-loaded into the data carrier my a manufacturer or distributor, while for other applications at least one of the identifier values comprises a patient identifier, or another meaningful value. For some applications, at least one of the information-bearing agent container and the patient-specific data carrier performs the detection of the correspondence, while for other applications the imaging system or another element of the end-to-end system performs the detection of the correspondence.

In some embodiments of the present invention, the imaging system comprises a SPECT imaging system configured to utilize the information contained in the

labeled radiopharmaceutical agent container and/or the patient-specific data carrier to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

The integration of the elements of the end-to-end system, and the exchange of authenticatable information among the elements generally increase patient safety, by ensuring that each patient receives the prescribed labeled radiopharmaceutical agent and dosage, and undergoes the desired imaging protocol. For some applications, one or more elements of the end-to-end system are configured to perform their respective function only upon being triggered by another element of the system. For example, the administration or imaging system may perform its function only upon being triggered by the information-bearing radiopharmaceutical agent container, by the patient-specific data carrier, and/or, in the case of the administration system, by the imaging system.

In some embodiments of the present invention, the automated radiopharmaceutical dispensing system comprises an information manager that is configured to receive radiopharmaceutical information regarding a labeled radiopharmaceutical agent and patient information regarding a patient. Responsively to the information, the dispensing system automatically dispenses a dose of the labeled radiopharmaceutical agent to an agent container, and stores the radiopharmaceutical information and at least a portion of the patient information in a data carrier associated with the container. For some applications, the radiopharmaceutical information is selected from the group consisting of: imaging protocol information for use with the labeled radiopharmaceutical agent, such as a SPECT imaging protocol; at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent; and authenticatable information regarding a commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

In some embodiments of the present invention, the dispensing system is configured to receive a mother vial containing a labeled radiopharmaceutical agent in

a quantity sufficient for preparation of a plurality of doses of the labeled radiopharmaceutical agent. Associated with the mother vial is a data carrier containing information regarding the labeled radiopharmaceutical agent, such as the formulation, radioactivity information, and protocol information. The information manager of the dispensing system receives at least a portion of the labeled radiopharmaceutical agent information from the data carrier.

In some embodiments of the present invention, use of the end-to-end automated system enables customization of one or more aspects of the imaging process, from dispensing to diagnosis. Customization typically includes one or more of the following:

The dispensing system customizes the dispensed dose for a specific patient, based on radiopharmaceutical information and patient-specific information. Typically, the dispensing system customizes the dispensed dose (e.g., the radioactivity level thereof) based in part on the scheduled time of the scheduled time of administration of the dose, and/or the scheduled time of the imaging procedure to be performed using the dose.

The administration system customizes the administered dose for a specific patient, based on radiopharmaceutical information and patient-specific information. For some applications in which the administration system customizes the administered dose, the radiopharmaceutical agent container contains a standard, non-customized dose.

The imaging system customizes image acquisition, image reconstruction, image analysis, and/or diagnosis, based on radiopharmaceutical information and patient-specific information, such as patient physiology and/or known and/or suspected disease of the patient.

Such customization is typically based at least in part on information provided by the manufacturer or distributor of the radiopharmaceutical agent. Such information may be in the form of lookup tables and/or expert system rules. A more detailed review of the customization parameters is provided hereinabove.

Of note, the term "labeled" means radiolabeled, and "unlabeled" means not radiolabeled.

There is therefore provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

For some applications, the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

For some applications, the data carrier additionally contains administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

In an embodiment, the imaging protocol information comprises instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent. Alternatively or additionally, the imaging protocol information comprises an identifier of an imaging protocol. Further alternatively or additionally, the imaging protocol information comprises a parameter of the at least one labeled radiopharmaceutical agent. Still further alternatively or additionally, the imaging protocol information comprises a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

In an embodiment, the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information. Alternatively, the container contains a plurality of labeled radiopharmaceutical agents mixed together. For some applications, the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of labeled radiopharmaceutical agents.

In an embodiment, the data carrier comprises a first data carrier, which contains a first identifier value, the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values. For some applications, at least one of the first and second data carriers is configured to perform the detection of the correspondence.

Alternatively or additionally, the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

In an embodiment, at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications, at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, exactly one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one labeled radiopharmaceutical agent.

In an embodiment, the data carrier is physically coupled to the container. For some applications, the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and the imaging protocol information comprises imaging protocol information selected for the patient. For some applications, the imaging protocol information comprises an identifier of an imaging protocol.

For some applications, the imaging protocol information comprises imaging protocol information customized for the patient. Custmization is described elsewhere in the application.

Description of the imaging system which may be used in the present system is provided in Example 3 hereinabove.

In an embodiment, the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study, and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the labeled

radiopharmaceutical agent is to be administered. For some applications, the data carrier comprises a coupling mechanism configured to be coupled to the patient. In an embodiment, the data carrier comprises a first data carrier, and wherein the apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent.

There is also provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

In an embodiment, the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

For some applications, the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

For some applications, the data carrier is physically coupled to the container.

There is further provided, in accordance with an embodiment of the present invention, apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

For some applications, the data carrier additionally contains patient information regarding a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

For some applications, the authenticatable license information is encrypted.

In an embodiment, the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

For some applications, the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

For some applications, the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

There is still further provided, in accordance with an embodiment of the present invention, apparatus comprising:

a first portable computer-communicatable data carrier containing a first identifier value;

a second portable computer-communicatable data carrier containing a second identifier value; and

an imaging system comprising imaging functionality, the imaging system configured, responsively to a detection of a correspondence between the first and second identifier values, to drive the imaging functionality to perform an imaging procedure on a patient.

For some applications, at least one of the first and second data carriers is configured to perform the detection of the correspondence. Alternatively or additionally, the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

For some applications, at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications, at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications, the apparatus comprises a device configured to write at least one of the first and second identifier values to the respective first and second data carriers.

In an embodiment, at least one of the first and second data carriers contains radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the imaging system comprises a communication element, configured to read the radiopharmaceutical information from the at least one of the data carriers, and the imaging system is configured to configure the imaging procedure at least in part responsively to the read radiopharmaceutical information. For some applications, the apparatus comprises a container containing the at least one labeled radiopharmaceutical agent. For some applications, one of the first and second data carriers is physically coupled to the container.

In an embodiment, the imaging functionality comprises a nuclear camera. For some applications, the nuclear camera comprises a SPECT camera.

There is yet further provided, in accordance with an embodiment of the present invention, apparatus for use with first and second portable computer-communicatable data carriers containing first and second identifier values, respectively, the apparatus comprising an imaging system, which comprises:

imaging functionality; and

a control unit configured to drive the imaging functionality to perform an imaging procedure on a patient, responsively to a detection of a correspondence between the first and second identifier values.

For some applications, the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

There is additionally provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

a' second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

For some applications, the imaging protocol information comprises SPECT imaging protocol information.

For some applications, the patient information comprises an identifier of the patient.

For some applications, the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

For some applications, the first data carrier contains a first patient identifier, the patient information contained in the second data carrier comprises a second patient identifier, and the apparatus comprises an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

a second communication element, configure to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the first data carrier contains a first protocol identifier, the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and the apparatus comprises an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that

triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the first data carrier contains a first protocol identifier, the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and the apparatus comprises an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

In an embodiment, the apparatus comprises an administration system, which comprises:

a communication element; and

a control unit, configured to:

generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container, and

drive the communication element to transmit information regarding the administration to the second data carrier.

For some applications, the apparatus comprises a device configured to write the imaging protocol information to the first data carrier. Alternatively or additionally, the apparatus comprises a device configured to write the patient information to the second data carrier.

In an embodiment, the imaging protocol information comprises imaging protocol information selected for the patient. For some applications, the imaging protocol information comprises an identifier of an imaging protocol. For some applications, the imaging protocol information comprises imaging protocol information customized for the patient.

In an embodiment, the first data carrier contains a first patient identifier, the patient information contained in the second data carrier includes a second patient identifier, and the apparatus comprises an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the administration system comprises an automated administration device, configured to administer the at least one labeled radiopharmaceutical agent to the patient upon being triggered by the administration signal.

For some applications, the control unit is configured to generate the administration signal to trigger the administration of the at least one labeled radiopharmaceutical agent by instructing a healthcare worker to administer the at least one labeled radiopharmaceutical agent to the patient.

There is yet additionally provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the labeled radiopharmaceutical agent and the patient; and

a SPECT imaging system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the data carrier contains the data regarding the labeled radiopharmaceutical agent. Alternatively or additionally, the data carrier contains the data regarding the patient.

For some applications, the control unit is configured to utilize the read data to customize the administration of the labeled radiopharmaceutical agent. Alternatively or additionally, the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered. Further alternatively or additionally, control unit is configured to utilize the read data to customize the reconstruction of the SPECT image. Still further alternatively or additionally, the control unit is configured to utilize the read data to customize the analysis of the SPECT image. Alternatively or additionally, the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the apparatus comprises a device configured to write the data to the data carrier.

There is also provided, in accordance with an embodiment of the present invention, a SPECT imaging system for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the system comprises a device configured to write the data to the container.

There is further provided, in accordance with an embodiment of the present invention, an automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container, the system comprising:

a robot, configured to manipulate the container;

a communication element; and

a control unit, configured to:

receive radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent,

receive patient information regarding a patient,

drive the robot to automatically dispense a dose of the labeled radiopharmaceutical agent to the container, and

drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

For some applications, the control unit is configured to receive the radiopharmaceutical information regarding a plurality of labeled radiopharmaceutical agents, and drive the robot to automatically dispense respective doses of the labeled radiopharmaceutical agents to the container.

For some applications, the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

For some applications, the control unit is configured to drive the communication element to transmit to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

In an embodiment, the apparatus comprises:

a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof; and

a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information,

wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

For some applications, the radiopharmaceutical information comprises the imaging protocol information. For some applications, the imaging protocol information comprises SPECT imaging protocol information, which may comprise at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

In an embodiment, the radiopharmaceutical information comprises the authenticatable information regarding the commercial license. For some applications, the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent. For some applications, the control unit is configured to authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

There is still further provided, in accordance with an embodiment of the present invention, apparatus for use with a container, the apparatus comprising:

a mother vial having a volume of at least 10 ml, which contains at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and at least 5 ml of saline solution; and

an automated radiopharmaceutical dispensing system, configured to contain the mother vial, and to dispense at least one dose from the mother vial to the container.

There is additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a portable computer-communicatable data carrier with the container; and

writing, to the data carrier, imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

There is yet additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a computer-communicatable data carrier with the container; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

There is also provided, in accordance with an embodiment of the present invention, a method comprising:

providing a portable computer-communicatable data carrier; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

There is further provided, in accordance with an embodiment of the present invention, a method comprising:

writing first and second identifier values to first and second computer-communicatable data carriers, respectively;

detecting a correspondence between the first and second identifier values; and

perform an imaging procedure on a patient responsively to the detecting.

There is still further provided, in accordance with an embodiment of the present invention, a method for use with at least one labeled radiopharmaceutical agent for administration to a patient, the method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

physically coupling a first computer-communicatable data carrier to the container;

writing, to the first data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

writing, to a second portable computer-communicatable data carrier, patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

There is additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing, in a container, at least one labeled radiopharmaceutical agent for administration to a patient;

associating a computer-communicatable data carrier with the container;

writing data to the data carrier regarding at least one of: the labeled radiopharmaceutical agent and the patient;

reading the data from the data carrier at a SPECT imaging system;

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical

agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

There is yet additionally provided, in accordance with an embodiment of the present invention, a method for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the method comprising: reading the data at a SPECT imaging system; and

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

There is also provided, in accordance with an embodiment of the present invention, a method for use with a container and a computer-communicatable container data carrier associated with the container, the method comprising:

receiving, by an automated radiopharmaceutical dispensing system, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent;

receiving, by the dispensing system, patient information regarding a patient;

automatically robotically dispensing, by the dispensing system, a dose of the labeled radiopharmaceutical agent to the container; and

transmitting to the container data carrier, by the dispensing system, at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

There is further provided, in accordance with an embodiment of the present invention, a method for automatically dispensing a labeled radiopharmaceutical agent to a container, comprising:

providing a mother vial having a volume of at least 10 ml;

filling the mother vial with at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and with at least 5 ml of saline solution;

placing the mother vial in an automated radiopharmaceutical dispensing system; and

dispensing at least one dose from the mother vial to the container.

There is also provided, in accordance with an embodiment of the present invention, a method for setting a dose of a labeled radiopharmaceutical agent for use for performing an imaging procedure on a patient for studying a physiological characteristic of the patient, the method including:

selecting the radiopharmaceutical agent;

receiving information regarding a medical parameter of the patient not directly related to the physiological characteristic of the patient; and

setting the dose at least in part responsively to the received information.

There is further provided, in accordance with an embodiment of the present invention, a substance associated with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is still further provided, in accordance with an embodiment of the present invention, a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter, for indicating a time-dependent substance intake program.

There is yet further provided, in accordance with an embodiment of the present invention, a substance associated with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is also provided, in accordance with an embodiment of the present invention, a time-dependent substance intake program generated by a computer

controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is further provided, in accordance with an embodiment of the present invention, a substance formulated in accordance with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is still further provided, in accordance with an embodiment of the present invention, an apparatus, method, and/or functionality for generation of a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter, including providing a time-dependent substance intake program; a data acquisition system which acquires data from the patient passing through the intake program; and a computerized analysis using a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is yet further provided, in accordance with an embodiment of the present invention, an apparatus, method, and/or functionality for generation of a human physiological profile, including providing a substance intake program; a data acquisition system which acquires data from the patient passing through the intake program; and a computerized analysis using a substance profile, including at least one kinetic parameter.

There is also provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable information-bearing, customized medicine module suitable for use in computerized customized medicine, said customized medicine module including a computerized customized medicine machine-interfaceable pharmaceutical-containing delivery module and a computerized individualized medicine machine-readable information-containing carrier containing at least data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized customized medicine, said data being useful

in computerized customized medicine machine actuation of said pharmaceutical-containing delivery module.

There is additionally provided, in accordance with an embodiment of the present invention, a computerized customized medicine machine including:

a computerized patient imager;

a computerized pharmaceutical deliverer employing a pharmaceutical-containing, machine-readable information-bearing, customized medicine module; and

a customized medicine protocol controller including:

an interactive patient imager interface including patient information receiving functionality and patient imaging actuation functionality; and

an interactive pharmaceutical deliverer interface including patient information receiving functionality and patient information-responsive pharmaceutical delivery actuation functionality.

There is also provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable authenticated, authenticated customized medicine module suitable for use in computerized customized medicine, said customized medicine module including a computerized customized medicine machine-interfaceable pharmaceutical-containing module and a computerized individualized medicine machine-readable authentication-containing carrier containing at least authentication data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized customized medicine, said data being useful in said computerized customized medicine machine.

There is further provided, in accordance with an embodiment of the present invention, a computerized customized medicine preparation machine including:

a computerized patient information manager;

a computerized customized medicine pharmaceutical information manager;

a computerized authenticated customized medicine module authenticator; and

a computerized pharmaceutical-containing, machine-readable information-bearing, customized medicine module generator including:

a computerized generator protocol manager operative to receive patient information from said patient information manager, to receive authentication of an authenticated customized medicine module from said authenticator, to receive customized medicine pharmaceutical information relating to at least one

pharmaceutical contained in said authenticated customized medicine module from said pharmaceutical information manager and to prepare customized medicine information to be included in said customized medicine module; and

a computerized pharmaceutical-containing, machine-readable information-bearing, customized medicine module preparer operative to associate said customized medicine information prepared by said protocol manager in an authenticatable machine readable form with a quantity of said pharmaceutical contained in said authenticated customized medicine module, thereby providing a pharmaceutical-containing, machine-readable information-bearing, customized medicine module.

There is still further provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable information-bearing, individualized medicine module suitable for use in computerized individualized medicine, said individualized medicine module including a computerized individualized medicine machine actuable pharmaceutical-containing delivery module and a computerized individualized medicine machine-readable information-containing carrier containing at least data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized individualized medicine, said data being useful in computerized individualized medicine machine actuation of said pharmaceutical-containing delivery module.

For some applications, said data is in an encrypted format, readable by said computerized individualized medicine machine upon receipt of a predetermined authentication.

There is also provided, in accordance with an embodiment of the present invention, a computerized individualized medicine machine including:

a computerized patient imager;

a computerized pharmaceutical deliverer employing a pharmaceutical-containing, machine-readable information-bearing, individualized medicine module; and

an individualized medicine protocol controller including:

an interactive patient imager interface including patient image receiving functionality and patient imaging actuation functionality; and

an interactive pharmaceutical deliverer interface including patient image receiving functionality and patient image-responsive pharmaceutical delivery actuation functionality.

There is further provided, in accordance with an embodiment of the present invention, use of a high definition, high sensitivity camera for determination of an optimal parameter for a labeled radiopharmaceutical agent, the optimal parameter selected from the group consisting of: optimal dose, optimal mode of administration, optimal mode of acquisition of data with respect to the labeled radiopharmaceutical agent, optimal mode of data processing with respect to the labeled radiopharmaceutical agent, and optimal mode of presentation of information acquired with respect to the labeled radiopharmaceutical agent.

There is still further provided, in accordance with an embodiment of the present invention, a labeled radiopharmaceutical agent that is manufactured or designed or indicated for use with or sold with any one of the above techniques.

EXAMPLE 5
IMAGING SYSTEM

As mentioned hereinabove, the present invention relates to radioimaging cameras characterized by unprecedented high sensitivity allowing for high resolution image acquisition for use in clinical diagnostic protocols algorithms described hereinwbove and systems operable in conjunction with the camera, the algorithms and systems include, but are not limited to, predetermined view selection algorithm and system, active vision (on the fly view selection) algorithm and system, closed loop administration of a radiopharmaceutical algorithm and system, expert system diagnostic algorithm and system, automatic dose preparation algorithm and kinetic parameter extraction algorithm and system; low dose radiopharmaceuticals; combinations of radiopharmaceuticals either as compositions (cocktails) and/or kits; an administering device of radiopharmaceuticals, which may include syringes, pumps and IV lines; mixers for mixing different radiopharmaceuticals; and an ERP system for controlling and monitoring each one or more of the above.

The present invention emerges from the development of a radioimaging camera characterized by unprecedented sensitivity. The sensitivity of the camera is attributed, as is further detailed hereinbelow, to at least the following constructual

features: (a) a plurality of detecting units; (b) movability of the detecting units one with respect to the other; (c) thus allowing concentrated focus on a region-of-interest by the individual detecting units; and (d) wiring diagram with minimal multiplexing, thereby preventing saturation thereof.

As a result of this sensitivity, it is now possible using the camera of the present invention to (a) detect low dose radiopharmaceuticals; (b) perform fast kinetic studies; (c) extract kinetic parameters for the distribution of a radiopharmaceutical under different diagnostic setups, thereby allowing (i) formulating radiopharmaceuticals based on the newly achieved knowledge of the kinetic parameters; (ii) diagnostics based on the kinetic parameters; (iii) formulating new therapeutic drugs based on the kinetic parameters; and (iv) using the kinetic parameters as an input to the expert system for diagnostics; (d) provide images of co-administered radiopharmaceuticals; and (e) allow diagnostically meaningful imaging at a far faster rate as compared to conventional prior art radioimaging cameras.

In order to minimize the exposure of a subject to radioactive substances and in order to maximize the diagnostic capabilities using radioimaging, the inventors of the present invention developed low dose preparations of radiopharmaceuticals and compositions and kits comprising two or more radiopharmaceuticals adapted for use in conjunction with the camera and all other aspects of the invention (See Example 1 and 2).

Basic imaging concept

Figures 1A and 1B schematically illustrate a detecting unit 12 and a block 90 of detecting units 12, respectively.

As seen in Figure 1A, the detecting unit 12 is formed of a single-pixel detector 91, having a thickness τ_d and a diameter D or, in the case of a non-circular detector, a diameter equivalent. Alternatively, several pixels may be summed up so as to operate, in effect, as a single pixel. Both the detector diameter D and the detector thickness τ_d affect the detecting efficiency. The detector diameter D determines the surface area on which radioactive emission impinges; the greater the surface area, the greater the efficiency. The detector thickness τ_d affects the stopping power of the detector. High-energy gamma rays may go through a thin detector; the probability of their detection increases with an increase in the detector thickness τ_d.

Figure 1A illustrates a single-pixel detector 91, which by itself cannot generate an image; rather, all counts are distributed over the surface area of the detector 91.

As seen in Figure 1B, the block 90 includes a plurality of the detecting unit 12, formed by dividing the detector 91 into a plurality of electrically insulated pixels 106, each associated with a collimator 96. The collimators 96 are of the diameter or diameter equivalent D, a length L, and a septum thickness τ. The collimators 96 may be, for example, of lead, tungsten or another material which substantially blocks gamma and beta rays. The collimators 96 may be shaped as tubes, rectangular grids, or grids of anyother polygon. Wide-angle or narrow-angle collimators are also possible.

The collimator's geometry and specifically, the ratio of D/L, provides the detecting unit 12 with a collection solid angle δ analogous to the viewing solid angle of an optical camera. The collection solid angle δ limits the radioactive-emission detection to substantially only that radioactive emission which impinges on the detector 91 after passing through a "corridor" of the collimator 96 (although in practice, some high-energy gamma rays may penetrate the collimator's walls). With no collimator, the collection angle δ, is essentially a solid angle of 4π steradians.

Thus, the collimator's geometry affects both the detection efficiency and the image resolution, which are defined as follows:

i. The detection efficiency is the ratio of measured radiation to emitted radiation; and

ii. The image resolution is the capability of making distinguishable closely adjacent manifestations of a pathology, or the capability to accurately determine the size and shape of individual manifestations of a pathology.

While it is naturally desired to optimize both the detection efficiency and the image resolution, they are inversely related to each other. The detection efficiency increases with an increase in the collimator collection angle, and the image resolution decreases with an increase in the collimator collection angle.

In other words, while a wide-aperture, single-pixel detecting unit, such as that of Figure 1A provides high efficiency, it does not lend itself to the generation of a two-dimensional image, and the wide aperture blurs the information regarding the direction from which the radiation is emitted. Yet as the resolution is increased, for example, in the detecting unit 12 of Figure 1B, the detection efficiency decreases.

Commonly owned US Applications 20040015075 and 20040054248 and commonly owned PCT publication WO2004/042546, all of whose disclosures are incorporated herein by reference, describe systems and methods for scanning a radioactive-emission source with a radioactive-emission camera of a wide-aperture collimator and, at the same time, monitoring the position of the radioactive-emission camera, at very fine time intervals, to obtain the equivalence of fine-aperture collimation. In consequence, high-efficiency, high-resolution images of a radioactivity emitting source are obtained. This is discussed below with regard to Figures 2 – 3B.

Figure 2 schematically illustrates the basic component of a system 120 comprising a radioactive-emission camera 122, operative as a detection system, and a position-tracking device 124, both in communication with a data-processing system 126. The radioactive-emission camera 122 is associated with a first coordinate system 128, and the position-tracking device 124 is associated with a second coordinate system 128', wherein the position-tracking device 124 monitors the position of the radioactive-emission camera 122 as a function of time. The data-processing system 126 processes the measurements of both the radioactive-emission camera 122 and the position-tracking device 124 and combines them to form the image.

Figure 3A schematically illustrates a manner of operating the radioactive-emission camera 122 with the position-tracking device 124 of the system 120. The radioactive-emission camera 122 moves about an area of radioactive emission 110, for example, in the direction of an arrow 118, so as to measure a radioactive emission distribution 112, as a function of time, while the position-tracking device 124 monitors the position of the camera 122. The radioactive-emission camera 122 may be a single-pixel detector of high efficiency, which is incapable, by itself, of producing images. Nonetheless, a data-processing system 126 processes a radioactive-count-rate input 121 together with a position-tracking input 123, using algorithms 125, to reconstruct an image 110' of the area of radioactive emission 110 for example, on a display unit 129.

Imaging according to this concept is illustrated in Figure 3B. The area of radioactive emission 110 is located in a two-dimensional coordinate system u;v, and includes two hot points 115. The camera 122 moves from a position P(1), at a time

t(1), to a position P(2), at a time t(2), while measuring the radioactive emission distribution 112 of the area of radioactive emission 110, including the hot points 115.

An example of a suitable position-tracking device 124 for use with system 120 is the miniBird™, which is a magnetic tracking and location system commercially available from Ascension Technology Corporation, P.O. Box 527, Burlington, Vermont 05402 USA (http://www.ascension-tech.com/graphic.htm). The miniBird™ measures the real-time position and orientation (in six degrees of freedom) of one or more miniaturized sensors, so as to accurately track the spatial location of cameras, instruments, and other devices. The dimensions of the miniBird™ are 18 mm x 8 mm x 8 mm for the Model 800 and 10 mm x 5 mm x 5 mm the Model 500. Alternatively, other optical tracking systems which may be used are NDI-POLARIS of Northern Digital Inc., Ontario, Canada, which provides passive or active systems, a magnetic tracking device of NDI-AURORA, an infrared tracking device of E-PEN system, or an ultrasonic tracking device of E-PEN system. Additionally or alternatively, the position-tracking device may be an articulated-arm position-tracking device, an accelerometer-based position-tracking device, a potentiometer-based position-tracking device, or a radio-frequency-based position-tracking device.

Commonly owned US application 20040054248 and commonly owned PCT publication WO2004/042546 further disclose various extracorporeal and intracorporeal systems 120 wherein the position-tracking devices 124 associated with the radioactive-emission cameras 122 have relatively wide apertures. Examples of extracorporeal and intracorporeal radioactive-emission cameras of this type are seen in Figures 4A – 4C.

Figure 4A schematically illustrates one embodiment of system 120, including a hand-held, extracorporeal device 170, which includes the camera 122, having a detector 132 and a collimator 134. The system 120 also includes a controller 130 and a position-tracking device 124, wherein the camera 122 and the position-tracking device 124 are associated with the data-processing system 126 discussed above with reference to Figures 2 – 3B.

Figure 4B schematically illustrates another embodiment of system 120 wherein an intracorporeal camera device 180 includes the radioactive-emission camera 122 mounted on a catheter 136. The camera 122 includes the detector 132,the collimator 134, and the position-tracking device 124, wherein the camera 122 and the

position tracking device 124 are associated with the data-processing system 126 discussed above with reference to Figures 2 – 3B. The camera 122 is configured so as to penetrate a tissue 135, via a Trocar valve 138. A structural imager 137, such as an ultrasound imager or an MRI camera may further be included.

Figure 4C schematically illustrates yet another embodiment of system wherein an intracorporeal camera device 190 is adapted for rectal insertion. The device 190 includes the radioactive-emission camera 122, which includes a plurality of the detectors 132 and the collimators 134 associated with the position-tracking device 124. The intracorporeal 190 device may be further adapted for motion along the x and ω directions. For example, the intracorporeal device 190 may include a motor 154 for moving the device 190 in the x and ω directions, such that, once inserted into a rectum, it may be propelled therealong. A suitable motor 154 may be obtained, for example, from B-K Medical A/S, of Gentofte, DK, and may be adapted to transmit information to the data-processing system 126, regarding the exact position and orientation of the intracorporeal device. 190. In some embodiments, the motor 154 may be used_in place of the position-tracking device 124. Alternatively, it may be used in addition thereto. The intracorporeal device 190 may further include the structural imager 137, such as an ultrasound imager or an MRI.

Initial view determination

Predetermined Views, Based on a Model of a Body Structure

Definition of a view

Referring now to the drawings, Figures 5A – 5F present the principles of modeling, for obtaining an optimal set of views, in accordance with embodiments of the present invention.

Figure 5A schematically illustrates a body section 230 having a region-of-interest (ROI) 200. The region-of-interest 200 may be associated with a body structure 215 having a specific radioactive-emission-density distribution, possibly suggestive of a pathological feature, this feature termed herein organ target 213. Additionally, there may be certain physical viewing constraints associated with the region-of-interest 200.

In accordance with embodiments of the present invention, Figure 5C illustrates, in flowchart form, a method 205 for best identifying an optimal and

permissible set of views for measuring the radioactive-emissions of the region-of-interest 200, such that a three-dimensional image thereof may be reconstructed. The method 205 includes the following steps:

in a box 206: modeling the region-of-interest 200 as a model 250 of a volume U, wherein U is the region-of-interest volume, and wherein the volume U may include one or several radioactive-emission sources, operative as modeled organ targets HS located within anatomical constraints AC, as seen in Figure 5B;

in a box 207: obtaining an optimal and permissible set of views for the modeled volume U Figure 5B; and

in a box 208: applying the optimal set of views to the in-vivo region-of-interest 200 and the body structure 215 of Figure 5A.

It will be appreciated that the model 250 of the region-of-interest 200 may be based on general medical information of the body structure 215 and common pathological features associated with it. Additionally, the model may be based on information related to a specific patient, such as age, sex, weight, and body type. Furthermore, in order to facilitate generation of the model 250, a structural image, such as by ultrasound or MRI, may be used for providing information about the size and location of the body structure 215 in relation to the body section 230.

Figures 5D – 5F schematically illustrate three types of the modeled organ targets HS, as follows:

i. a region of concentrated radiation, or a hot region, for example, as may be associated with a malignant tumor and as seen in Figure 5D;

ii. a region of low-level radiation, which is nonetheless above background level, for example, as may be associated with carcinoma and as seen in Figure 5E; and

iii. a region of little radiation, or a cold region, below the background level, for example, as may be associated with dead tissue and as seen in Figure 5F.

Referring further to the drawings, Figures 6A and 6B pictorially illustrate a view and viewing parameters associated therewith, in accordance with embodiments of the present invention.

Figure 6A illustrates the volume U, subdivided into voxels u. The volume U is defined in a six-degree coordinate system $x;y;z;\omega;\theta;\sigma$ having a point of origin $P0(x0; y0; z0; \omega0; \theta0; \sigma0)$. A detecting unit 102 is positioned at a location and orientation $P1(x1; y1; z1; \omega1; \theta1; \sigma1)$. The detecting unit 102 has a detector 104,

formed of a specific detector material having a thickness τ_d, and a collimator 108, having a diameter D and a length L and defining a collection angle δ.

Figure 6B schematically illustrates the emission rate of the volume U, as a function of time, given that a radioactive material of a specific half-life has been administered at a time T0.

A view may thus be defined as a group of nonzero probabilities of detecting a radioactive emission associated with all the voxels that form a sector S (Figure 6A). A view is sometimes referred to as a projection, and the two terms are synonymous. Furthermore, a view defined over a sector S can be naturally extended to be defined over the set of all voxels, by simply associating a zero probability with every voxel outside the sector S. This makes possible the application of mathematical operations over the entire volume U.

A view is dependent on the following viewing parameters:

Location and orientation parameters:

The location and orientation of the detecting unit 12 in a six-dimensional space, P1(x1; y1; z1; ω1; θ1; σ1), with respect to the origin P0(x0; y0; z0; ω0; θ0; σ0) of the volume U.

Detecting-unit parameters:

The collection angle δ which, together with the location and orientation parameters P1(x1; y1; z1; ω1; θ1; σ1) with respect to the origin P0(x0; y0; z0; ω0; θ0; σ0), define the sector S;

The detector material, which affects the detector efficiency;

The detector thickness τ_d, which affects the detector's stopping power, hence, its efficiency; and

The diameter of the detecting unit, or the effective diameter, calculated so as to produce a circle of the same area, when the geometry is not a circle.

Attenuation parameters:

Attenuation properties of all the voxels within the sector S, as they affect the probabilities that radioactive emissions from a specific voxel will reach the detector, wherein different voxels within the sector S may have different attenuation properties, since several types of tissue may be involved.

Radiopharmaceutical parameters:

The half life $t_{1/2}$ of the radiopharmaceutical, the types of radioactive emission, whether gamma or beta, and the energies of the radioactive emissions, which affect the probability of detection.

As used herein the phrase "kinetic profile" means a collection of one or more parameters descibing the rate of distributin due to flow, uptake, bioclerance, diffusion, active transport, metabolism and the like.

A kinetic profile is either definable in general or per patient, per organ, per tissue and under various contitions, such as pathologies and stimulations.

<u>Time parameters:</u>

T0 is the time of administrating the radiopharmaceutical, T1 is the time since administration, and the duration of the measurement is $\Delta T1$, which affects the number of emissions that occur during the radioactive-emission measurement.

Some of these viewing parameters are fixed for a particular situation. Specifically, the tissue attenuation parameters are given. Additionally, the time T1 since administration of the radiopharmaceutical is generally governed by the blood pool radioactivity, since it is generally necessary to wait until the blood pool radioactivity dies out for low-level detection to be possible. For the remaining viewing parameters, optimization may be carried out.

The remaining viewing parameters may be divided into two categories:

i. viewing parameters in the design of a radioactive-emission camera;

ii. viewing parameters for an optimal set of views, for a given camera.

Viewing Parameters for an Optimal set of Views, for a Given Camera

Referring further to the drawings, Figures 7A – 7C schematically illustrate anatomical constraints, which may hinder measurements.

Figure 7A schematically illustrates the region-of-interest 200, for which a three-dimensional radioactive-emission image is desired. The region-of-interest 200 is in free space, with no constraints to limit accessibility to it. Thus, a radioactive-emission camera 210 may travel, for example, along tracks 202 and 204, and any other track, unhindered.

In Figure 7B, the region-of-interest 200 is associated with the body structure 215, such as a prostrate, in vivo. For obtaining a radioactive-emission image, the

radioactive-emission camera 210 may be inserted transrectally, so as to travel in a rectum 206, for example, in the direction of an arrow 208. Its ability to image the prostrate is limited by anatomical constraints.

In Figure 7C, the region-of-interest 200 is associated with the body structure 215, such as a heart, a breast, or another organ, in vivo, and the radioactive-emission camera 210 may be an extracorporeal camera, which may perform radioactive-emission measurements from outside the body, on an extracorporeal surface 214, for example when moving along a track 212.

In each of these cases, it is desired that a reconstructed three-dimensional radioactive-emission image of the region-of-interest 200 be obtained at a predetermined quality. This is achieved by predefining an optimal set of radioactive-emission measurement views, tailored to the specific body structure 215 and optimized with respect to the information gained regarding the body structure 215.

Referring further to the drawings, Figure 8 illustrates, in flowchart form, a method 300 of predefining a set of views for functional imaging, tailored for imaging a specific body structure, and optimized with respect to the functional information gained about the body structure, in accordance with embodiments of the present invention. In effect, Figure 8 is an expansion of Figure 5C. The method 300 comprises:

in a box 302: providing a model of the body structure 215, based on its geometry;

in a box 304: providing a model of anatomical constraints, which limit accessibility to the body structure;

in a box 306: providing a collection of views of the modeled body structure obtained within the modeled anatomical constraints;

in a box 308: providing a scoring function, by which any set of at least one view, from a collection of views, is scorable with a score that rates information obtained from the modeled body structure by the set;

in a box 310: forming sets of views from the collection of views and scoring them with the scoring function; and

in a box 312: selecting a set of views, from the collection of views, based on their scores, as the predefined set of views.

The model of the body structure is based on anatomical knowledge regarding its size, shape, and weight. In fact, different models may be provided, for example, for different ages, sexes, weights, and body types, such as heavy-built, medium-built, or small-built. In accordance with a first embodiment, the body structure is modeled assuming that there is no radioactive emission throughout its volume. In accordance with other embodiments, the body structure may be modeled with one or more modeled organ targets, simulating different pathological features. Specifically, the modeled organ targets may be hot regions, of a radioactive-emission intensity higher than the background level, regions of low-level radioactive-emission intensity, which is nonetheless above the background level, and cold regions, of a radioactive-emission intensity lower than the background level. These may be distributed in accordance with medical records, which teach of sites within the body structure that may be more susceptible to certain pathologies.

Similarly, the model of anatomical constraints which limit accessibility to the body structure is based on anatomical knowledge, and different models may be provided, for example, for different ages, sexes, weights, and body types.

The collection of views may be obtained by several methods. It may be calculated analytically for the modeled body, based on the view parameters. Additionally or alternatively, computer simulations of the modeled body and the view parameters may provide the collection of views. Additionally or alternatively, measurements may be performed using a point source and a detecting unit of appropriate parameters, at different locations and orientations of the detecting unit, so as to simulate the desired geometries.

It will be appreciated that a combination of these may be used. For example, the measurements may be performed in air, but corrected analytically or by computer simulations, for tissue attenuation.

Referring further to the drawings, Figures 9A – 9F schematically illustrate possible models and collections of views for a body structure, in accordance with embodiments of the present invention.

Figure 9A schematically illustrates four views, formed by sectors S1, S2, S3, and S4 through the volume U, which has an even distribution of radioactive emission.

Figure 9B schematically illustrates three views, formed by sectors S1, S2, and S3, through the volume U, which includes a modeled pathological feature, which is the modeled organ target, HS.

Figure 9C schematically illustrates three views, formed by sectors S1, S2, and S3 through the volume U, which includes a modeled organ target, HS', of the same type as that of the modeled organ target HS, (that is, either a hot region or a cold region) but somewhat displaced along the x;y;z coordinate system. Additionally, the modeled organ target HS of Figure 9B is superimposed in Figure 9C, for illustrative purposes, in order to show the displacement, delta1, of modeled organ target HS' from modeled organ target HS.

Figure 9D schematically illustrates three views, formed by sectors S1, S2, and S3 through the volume U, which includes a modeled organ target, HS", of the same type as that of the modeled organ targets HS and HS', but somewhat displaced along the x;y;z coordinate system from them. Additionally, the modeled organ targets HS of Figure 9B and HS' of Figure 9C are superimposed in Figure 9D, for illustrative purposes, in order to show the displacements delta2 and delta3, vis a vis HS" of Figure 9D.

Figure 9E schematically illustrates three views, formed by sectors S1, S2, and S3 through the volume U, which includes two modeled organ targets, HS1 and HS2.

Figure 9F schematically illustrates four possible models of organs, shown as elliptical volumes, each with a slightly different distribution of modeled organ targets.

The modeled organ targets may be termed emmitance models. In general, an emmitance model is based on a particular radiopharmaceutical, which fixes both the rate of emission and the change in the rate of emission with time, determining the difference between the modeled organ target and the background level, as a function of time. To study the effect of different radiopharmaceuticals on the views, one may provide different emmitance models, based on different radiopharmaceuticals and different elapsed times relative to their administration.

The choice of an optimal set of views from among a collection of views, such as any of those illustrated in Figures 9A – 9E, is based on a scoring function, which rates different sets of views in terms of their information regarding the volume U. The scoring function is based on information theoretic measures that rate the quality of the data which each set of views provides.

Infotmation Theoretic Measures

A brief description of the information theoretic measures, upon which the scoring function may be based, is as follows:

Uniformity:

The information theoretic measure of uniformity requires that the probability of detecting a radioactive emission from each voxel, by one of the views, be substantially equal, i.e., substantially uniform for all the voxels.

This is illustrated with reference to Figure 9A. Basically, in one view, a voxel may have a high influence on the counts that are measured while, in another view, the same voxel may have a low influence on the counts that are measured. For example, consider a voxel u(1;1;1), in relation to the views associated with the sectors S2 and S4. The voxel u(1;1;1) has a high influence on the counts that are measured by the view associated with the sector S4, but a low influence on the counts that are measured by the view associated with the sector S2. The aim of uniformity is to identify a set of views that will balance the influence of each voxel for the entire set of views.

Separability:

The information theoretic measure of separability rates resolution, or the ability to distinguish between a pair of close models of the body structure, each having substantially identical dimensions, so as to define substantially identical volumes U having slightly different distributions of modeled organ targets.

For example, a pair of models of substantially identical volumes are illustrated in Figures 9B and 9C, wherein the respective modeled organ targets are HS, whose center is at a location $(x;y;z)_{HS}$ and HS', whose center is at a location $(x;y;z)_{HS'}$. As noted above, the displacement along the x axis is delta1, which may be measured, for example, in mm.

An optimal set of views, from the standpoint of separability, is that which will best distinguish between HS of Figure 9B and HS' Figure 9C. Thus, a score, in terms of separability, is given for the pair of models, the score relateing to a resolution as defined by the difference between the location of the two models. In the present example, the difference is delta1, so the score given by the information theoretic measure of separability will relate specifically to a resolution as defined by delta1

along the x-axis, relative to the locations of HS and HS'. Other portions of the volume U and other displacements may have different resolutions.

Additionally, as discussed above with regard to the model of Figure 9D, volume U includes the modeled organ target HS", whose center is at a location $(x;y;z)_{HS''}$. HS" is displaced from HS of Figure 9B, along the z-axis, the displacement denoted delta2, and is also displaced from HS' of Figure 9C, along the x- and z- axes, the displacement denoted delta3.

Scores, in terms of separability, may be given to all the pairing combinations, i.e., to the models of Figures 9B – 9C, with regard to delta1; to the models of Figures 9B – 9D, with regard to delta2; and to the models of Figures 9C – 9D, with regard to delta3. An optimal set of views may be selected based on the average scores for all the pairing combinations; for example, the optimal set may be that whose average score for all the pairing combinations is the highest. Alternatively, a weighted average may be applied.

It will be appreciated that more than one modeled organ target may be included in the volume U. It will be further appreciated that a set of views may be selected so as to provide high resolution for portions of the volume U known to be susceptible to pathologies, and so as to provide low resolution for portions of the volume U known to be generally free of pathological features.

With regard to Figure 9F, any pair of models of organs having different distributions of modeled organ targets, may be utilized for identifying an optimal set of views in terms of separability.

Reliability:

The information theoretic measure of reliability rates repeatability in measurement, so that repeated reconstructions are not substantially different. Reliability may be scored with respect to a single model of a body structure, having a specific distribution of modeled organ targets, for example, any one of the models of Figures 9B – 9E. Yet, preferably, several models of substantially identical volumes are provided, such as, for example, the four models of Figures 9B – 9E. Substantially identical sets of views may be applied to all the models and may be scored with respect to reliability. The optimal set is selected based on its average score for the plurality of the models. For example, the optimal set may be that whose average score for the plurality of the models is the highest.

The four models of organs of Figure 9F, each of which has a slightly different distribution of modeled organ targets, may also be used for identifying an optimal set of views in terms of reliability.

Weighted Combination:

A weighted combination of several information theoretic measures may also be used. For example, a plurality of models may be provided, all having substantially identical dimensions and volumes, as follows:

i. a first model of the volume U, free of modeled organ targets, as seen in Figure 9A, for scoring sets of views in terms of uniformity;

ii. at least one pair of models of the volume U, with slightly different distributions of modeled organ targets, as seen in any pair of Figures 9B - 9C, 9B – 9D, and (or) 9C - 9D, for scoring sets of views in terms of separability;

iii. at least one model of the volume U, with a given distribution of modeled organ targets, as seen in any one of Figures 9B, 9C, 9D, and (or) 9E, for scoring sets of views in terms of reliability.

Identical sets of views may be applied to all the models of the volume U, and each view may be scored in terms of uniformity, separability, and reliability. An optimal set of views may be selected based on a summation of the three scores, or based on a weighted average of the three scores.

The Greedy Construction

Some approaches for selecting an optimal set are based on determining a required quality of reconstruction, and finding a set of views that meets that requirement. Others are based on fixing the size for the set (i.e., the number of views in the set) and maximize the quality of the reconstruction for the given set size. Still other approaches define both a desired size for the set and a desired quality of reconstruction and search for a set of the desired size, which meets the desired quality of reconstruction.

However, given a desired size for a set of views and a desired quality of reconstruction, while it may be possible to search through all possible sets of the desired size, scoring each, in order to identify the set that meets the desired quality, the task may be monumental. For example, where the collection of views includes several thousand views, and a set size of 100 is desired, rating each combination of 100 views would be computationally impractical.

An alternative approach is the Greedy Construction. When applying the Greedy Construction, an information theoretic measure is chosen, for example, separability, and an initial set of a minimal number of views is defined. The set is gradually built up, so that with every addition, a view is picked so as to maximize the chosen information theoretic measure of the set.

This may be illustrated with reference to Figure 9E. Given that separability is the chosen information theoretic measure, and an initial set of view S1 is defined, the additions of views S2 and S3 may then be compared in order to determine with which of them separability is maximized. Intuitively, for the present example, the addition of S3 will maximize the chosen information theoretic measure of the set.

It will be appreciated that other scoring functions, as known, may similarly be used.

Performing Measurements

The advantage of the method of the present invention, of predefining a set of views based on a model of a body structure, using an information theoretic measure, so as to optimize the functional information from the views of the corresponding body structure, in vivo, becomes apparent when compared with the prior art alternatives. The prior art relies on obtaining random views, in vivo, or views dictated by anatomical constraints, with no rigorous approach to the manner by which they are chosen.

The method of the present invention, of predefining a set of views, based on a model of a body structure, using an information theoretic measure, so as to optimize the functional information from the views of the corresponding body structure, in vivo, is further illustrated hereinbelow, with reference to Figure 10.

Figure 10 illustrates, in flowchart form, a method 320 of functional imaging, tailored for imaging a body structure optimized with respect to the functional information gained about the body structure, by using the predefined optimal set of views, in accordance with embodiments of the present invention. The method 320 comprises:

in a box 322: providing a model of a body structure, based on its geometry;

in a box 324: providing a model of anatomical constraints, which limit accessibility to the body structure;

in a box 326: providing a collection of views of the modeled body structure, obtained within the modeled anatomical constraints;

in a box 328: providing a scoring function, by which any set of at least one view, from a collection of views is scorable with a score that rates information, obtained from the modeled body structure by the set;

in a box 330: forming sets of views from the collection of views and scoring them, with the scoring function;

in a box 332: selecting a set of views from the collection of views of the modeled body structure, based on its score, as the predefined set of views; and

in a box 334: performing radioactive-emission measurements of an in-vivo body structure that corresponds to the body structure that has been modeled, selectively at the predefined set of views.

It will be appreciated that the region-of-interest 200 may include an organ, such as a heart or a pancreas, a gland, such as a thyroid gland or a lymph gland, blood vessels, for example, the coronary artery or the pulmonary artery, a portion of an organ, such as a left atrium of a heart, a bone, a ligament, a joint, a section of the body, such as a chest or an abdomen, or a whole body.

A still more powerful approach may be achieved by taking the method of the present invention through second and third iterations, so as to zoom in on suspected pathological features that are identified. Specifically, when a suspected pathological feature is identified, a second, inner region-of-interest, limited to the region of the pathological feature and its surrounding anatomical structure, can be identified and modeled. An optimal pathology set of views, specifically for the second, inner region-of-interest, may be predefined, based on information theoretic measures, as before. This is illustrated hereinbelow, with reference to Figures 11 and 12.

Referring further to the drawings, Figures 11 pictorially illustrates a method 340 for zooming in on a suspected pathological feature, as a process of two or more iterations, in accordance with embodiments of the present invention, as follows:

In I: The region-of-interest 200, associated with the body structure 215, is defined for the body section 230.

In II: The model 250 of the volume U is provided for the region-of-interest 200, possibly with one or several of the modeled organ targets HS, and within the

anatomical constraints AC, for obtaining the optimal set of views for the region-of-interest 200. The optimal set of views is then applied to the body section 230.

In III: When a suspected organ target 213 is identified, in vivo, by radioactive-emission measurements at the optimal set of views, a second, inner region-of-interest 200' is defined, including the suspected pathological feature.

In IV: A model 250' of a volume U' is provided for the second, inner region-of-interest 200', preferably, with at least one modeled organ target HS, simulating the suspected organ target 213, for obtaining an optimal pathology set of views for the region-of-interest 200'. The second, pathology set of views is then applied to the body section 230.

Referring further to the drawings, Figure 12 illustrates, in flowchart form, the method 340, for zooming in on a suspected pathological feature of the body structure, as a process of two iterations, in accordance with embodiments of the present invention. The method 340 comprises:

in a box 342: providing a model of a body structure, based on its geometry;

in a box 344: providing a model of anatomical constraints, which limit accessibility to the body structure;

in a box 346: providing a first collection of views of the modeled body structure, obtained within the modeled anatomical constraints;

in a box 348: providing a first scoring function, by which any set of at least one view, from a collection of views, is scorable with a score that rates information, obtained from the modeled body structure by the set;

in a box 350: forming sets of views from the first collection of views, and scoring them, with the first scoring function;

in a box 352: selecting a set of views from the first collection of views of the modeled body structure, based on its score, as the predefined set of views;

in a box 354: performing radioactive-emission measurements of an in-vivo body structure that corresponds to the body structure that has been modeled, selectively at the predefined set of views;

in a box 356: identifying a suspected pathological feature, in the in-vivo body structure;

in a box 358: providing a model of the suspected pathological feature, based on its location in the body structure and general medical knowledge;

in a box 360: providing a model of the anatomical constraints, which limit accessibility to the suspected pathological feature;

in a box 362: providing a second collection of views of the modeled suspected pathological feature, obtained within the modeled pathology's anatomical constraints;

in a box 364: providing a second scoring function;

in a box 365: forming sets of views from the second collection of views, and scoring them, with the second scoring function;

in a box 366: selecting a set of pathology views from the second collection of views, based on its score, as the predefined pathology set of views; and

in a box 368: performing radioactive-emission measurements of the suspected pathological feature, selectively at the predefined pathology set of views.

It will be appreciated that the model of the suspected pathological feature may be provided responsive to a patient's complaint, a physician's examination, or based on input from another imaging system, for example, x-rays, CT, MRI, ultrasound, and gamma scanning, for example, with a hand-held gamma camera, rather then based on the findings of the first set of measurements, of the step 356, hereinabove.

Design of the Radioactive-emission camera

While the embodiments described with reference to Figures 5A – 12 relate to predefining a set of optimal views for a given radioactive-emission camera and a body structure, another side of the same coin relates to an optimal design of the radioactive-emission camera and camera system for the body structure, optimized with respect to functional information gained.

Thus, the embodiments described hereinbelow, with reference to Figures 13A – 15 illustrate methods of designing cameras and camera systems, optimized with respect to information gained about a body structure.

Referring further to the drawings, Figures 13A – 13E schematically illustrate possible designs of the radioactive-emission camera 10, and the process of obtaining views for a given camera design, in accordance with embodiments of the present invention.

Figures 13A – 13C schematically illustrate the radioactive-emission camera 10 as a radioactive-emission camera 226 arranged for measuring the radioactive-

emission-density distribution of three bodies, U1, U2 and U3. The volume U1 of Figure 13A has been modeled with no modeled organ targets, in order to score the radioactive-emission camera 226 in terms of uniformity. The volume U2 of Figure 13B includes two modeled organ targets, HS1 and HS2, and may be used for scoring the radioactive-emission camera 226 in terms of reliability. The volume U3 of Figure 13C includes two modeled organ targets, HS1 and HS2', so as to form a pair with the volume U2 of Figure 13B, and the pair may be used for scoring the radioactive-emission camera 226 in terms of separability. Additionally, the volume U3 may be used to obtain a second score in terms of reliability, and the two reliability scores may be averaged. It will be appreciated that additional bodies, of different radioactive emission density distributions may be used, for obtaining additional scores in terms of reliability, and for forming additional pairs, for additional scores in terms of separability, wherein the scores in terms of each scoring function may be averaged. Additionally, the scores of the three functions may be combined, for example, as a sum, or as a weighted average. It will be appreciated that only one of the scoring functions, or only two of the scoring functions may be used. Additionally or alternatively, another scoring function or other scoring functions may be used.

According to the present example, the camera 226 has two detecting units 222A and 222B whose collimators are arranged in parallel. The two detecting units 222A and 222B are adapted for motion in the directions of $\pm x$, within the camera 226, as shown by arrows 224 and 228, so as to provide coverage of a plane within the bodies U1 U2 and U3, in parallel sectors. Upon reaching the end of the travel in the $+x$ direction, as shown by the arrow 224, the two detecting units 222A and 222B may be rotated in the direction of ω, as shown by an arrow 217, and return in the $-x$ direction of the arrow 228. In this manner, complete coverage of the whole body is provided. A representative collection of views of the camera 226 may be defined as a set of views of the bodies U1, U2, and U3, taken at predetermined increments of Δx and $\Delta\omega$.

Intuitively, a set formed of parallel sectors may score poorly in terms of uniformity since radioactive emissions from voxels closer to the detecting unit have higher probabilities of being detected than radioactive emissions from voxels far from the detecting unit. Additionally, a set formed of parallel sectors may score poorly in

terms of separability, since it cannot distinguish between two models, which only differ in the depth of a pathological feature, along the z-axis.

Figure 13D schematically illustrate the radioactive-emission camera 10 as a radioactive-emission camera 220, arranged for measuring the radioactive-emission-density distribution of the volume U2, which may be used for scoring the radioactive-emission camera 220 in terms of reliability.

The camera 220 has the two detecting units 222A and 222B, arranged to sweep a plane within the volume U2, in a windshield-wiper-like manner, along $\pm\theta$, as illustrated by arrows 216 and 218. When sweeping along $\pm\theta$ is completed, the detecting units 222A and 222B rotate a few degrees along ω, as illustrated by the arrow 217, and sweeping along $\pm\theta$ is repeated in the new orientation. In this manner, coverage of the whole volume U2 is performed, from two locations and a large plurality of orientations. A representative collection of views of the camera 220 may be defined as a set of views of the volume U2, taken at predetermined increments of $\Delta\theta$ and $\Delta\omega$.

The significance of the present embodiment, is as follows:

i. The different detecting units 222A and 222B provide views from different orientations; and

ii. The different detecting units 222A and 222B may change their view orientations.

A score may be applied to this set, based on the information theoretic measure of reliability.

It will be appreciated that similarly, the camera 220 may be arranged for measuring the radioactive-emission-density distribution of the volume U1 (Figure 13A) and of the volume U3 (Figure 13C), and possibly also of other bodies, in order to score the radioactive-emission camera 220 also in terms of uniformity and separability. The scores of the three functions may be combined, for example, as a sum, or as a weighted average. It will be appreciated that only one of the scoring functions, or only two of the scoring functions may be used. Additionally or alternatively, another scoring function or other scoring functions may be used.

Intuitively, the set of representative collection of views of the present example is likely to score more highly in terms of separability than that of the camera 226 of Figure 13A, as it provides views from different locations and orientations.

In Figure 13E the detecting units 222A and 222B of the camera 220 are further adapted for motion in the directions of ±x, within the camera 220, as shown by the arrows 224 and 228.

Intuitively, the set of representative collection of views of the present example is likely to score more highly in terms of all three information theoretic measures, than those of the camera of Figures 13A – 13C and of the camera of Figure 13D, as the present example provides views from a large plurality of locations and orientations.

In this manner, the information theoretic measures may be used for scoring representative collections of views of suggested camera designs, and an optimal camera design may be chosen based on this score, as described hereinbelow, with reference to Figure 14, hereinbelow.

Figure 14 illustrates, in flowchart form, a method 370 for identifying a camera optimized with respect to information gained about the body structure. The method 370 comprises:

in a box 372: providing a model of a body structure, based on its geometry;

in a box 374: providing a model of anatomical constraints, which limit accessibility to the body structure;

in a box 375: providing representative collections of views of the modeled body structure, within the modeled anatomical constraints, for different camera designs;

in a box 376: providing a scoring function, by which each representative collection of views, associated with a specific camera design, is scorable with a score that rates information, obtained from the body structure;

in a box 377: scoring the representative collections of views, with the scoring function; and

in a box 378: selecting a camera design, based on the score of its representative collection of views.

In this manner, a comparison of the quality of the data that may be produced by each camera design can be made. This analysis is important at the camera-design stage, in order to eliminate situations where views which are anatomically possible and which are desired from the standpoint of information theoretic measures, are unattainable because of camera design limitations. For example, the camera 190 of

Figure 4C, hereinabove, cannot be used for the windshield-wiper-like motion, shown in Figure 13D, by the arrows 216 and 218; however, this type of coverage has proved very valuable. The method 370 may, however, be suitable for another camera design.

Additionally, when selecting a camera design, it is generally desired to consider secondary issues, such as the rate of data collection, the cost of the camera, the complexity of the design, for example, in terms of the number of motors, motion-transfer systems, and the like.

The rate of data collection is important both because it may be associated with patient discomfort and because it affects the number of patients that may be examined in a period of time. Where data collection with one camera design may take an hour and with another camera design may take 10 minutes, the design of the faster camera is highly advantageous. Complexity and cost are important because they affect the accessibility of the camera to the general public.

Thus, a design scoring function may be provided, for rating each camera design with a design score, based on any one or a combination of the secondary issues. The design scoring function may be used for selecting a camera design from several that have been found acceptable in terms of the quality of the data, by the method 370 of Figure 14.

Referring further to the drawings, Figure 15 illustrates, in flowchart form, a method 380 of selecting a camera design, optimized with respect to information gained about a body structure and secondary issues, in accordance with embodiments of the present invention. The method 380 comprises:

in a box 382: providing a model of a body structure, based on its geometry;

in a box 384: providing a model of anatomical constraints, which limit accessibility to the body structure;

in a box 385: providing representative collections of views of the modeled body structure, within the modeled anatomical constraints, for different camera designs;

in a box 386: providing a scoring function, by which each representative collection of views, associated with a specific camera design, is scorable with a score that rates information, obtained from the body structure;

in a box 387: scoring the representative collections of views, with the scoring function;

in a box 388: identifying several camera designs as acceptable, based on the scores of their representative collections of view;

in a box 390: providing a design scoring function, by which each camera design is scorable, based on the secondary issues;

in a box 392: scoring the acceptable camera designs with a design score;

in a box 394: selecting a camera design, based on its design score.

It will be appreciated other manners of combining the scoring function, which rates information, and the design scoring function, which rates secondary issues, are possible. For example, a combined scoring function, which takes all these factors into account, may be used.

As will be shown, hereinbelow, with reference to Figures 18A – 22X, many different camera designs may provide substantially the same information, but are different in terms of their secondary considerations, that is, at different rates of data collection, different costs and different complexity of their designs, for example, in terms of the number of motors and motion-transfer systems. Thus these may score similarly in terms of functional information, and a design scoring function may be used to choose from amongst them.

Referring further to the drawings, Figures 16A – 16L schematically illustrate viewing the elliptical model 250 of the volume U, with the camera 10, as illustrated specifically in Figures 20A – 20H, hereinbelow.

Figures 16A – 16K show the spanning of the elliptical model 250 of the volume U, along an x-z plane, by the sweeping views. Figure 16L is a pictorial representation of the camera 10 of Figures 20A – 20H and the elliptical model 250 of the volume U, in accordance with embodiments of the present invention.

The views, obtained in Figures 16A – 16K may be used both for:

i. a collection of views for the volume U, from which an optimal set of views may be chosen, specific to a body structure, in accordance with the teachings of Figures 8, 10, and 12, hereinabove, and

ii. a representative collection of views of the camera 10, for optimizing a camera design, in accordance with the teachings of Figures 14 and 15, hereinabove.

Imaging Schemes - Stop-Go, Interlacing and Continuous Acquisition

According to embodiments of the present invention there may be several imaging schemes connected with the motion of the detecting units, blocks and/or assemblies as follows:

In a first embodiment the detecting units, blocks and/or assemblies are moved to a position and collect photon emission data while stationary (herein referred to as the Stop-Go imaging scheme).

In a second embodiment, a version of the Stop-Go imaging scheme, a motion of each detecting unit or block or assembly is at a predetermined angle per move (after each move data is collected while the detecting unit or block or assembly is stationary) and characterized by half the angle phase shift when scanning in opposite directions, so as to scan the scanned region every half angle (herein referred to as the Interlacing imaging scheme).

In a third embodiment a motion of each detecting unit or block or assembly is without pause between minimum and maximum sweeping angles (herein referred to as the Sweeping Imaging Scheme).

Prescanning

Oftentimes it is desirable to perform a fast prescan of a subject undergoing diagnosis, find a region-of-interest, thereafter collect higher quality data from the region-of-interest. A prescan according to embodiments of the present invention can be performed by any imaging device, including, but not limited to, ultrasound and MRI or by a physical inspection of the subject undergoing diagnosis. Alternatively, a prescan can be performed by the camera of the present invention preferably using the interlacing imaging scheme as is further described above or by broad view selection as is further described below.

Examples of camera systems

Reference is now made to the following examples of radioactive-emission cameras and camera systems, for a comparative study taught with reference to Figures 14 and 15.

EXAMPLE 1A

Referring further to the drawings, Figures 18A and 18B schematically illustrate the radioactive-emission camera 10, of the single detecting unit 12 (see Figures 1A and 17A). The single detecting unit 12 has a motion with respect to the overall structure 20, which is a combination of a rotational motion around the x-axis, in the direction of ω, denoted by an arrow 44, and a translational motion along the x-axis, denoted by an arrow 46.

As a consequence, a spiral trace 48 is formed, for example, on an inner surface of a body lumen 232, as seen in Figure 18B.

Preferably, the motions of the detecting unit 12 are contained within the overall structure 20, so that the external surface of the camera 10 remains stationary. The external surface of the camera may be formed of a carbon fiber, a plastic, or another material, which is substantially transparent to nuclear radiation.

EXAMPLE 2A

Referring further to the drawings, Figures 18C and 18D schematically illustrate the radioactive-emission camera 10, of the single block 90 (Figures 1B and 17E). Note that all the detecting units 12 of the single block 90 move as a single body. The single block 90 has a motion with respect to the overall structure 20, which is a combination of the rotational motion around the x-axis, in the direction of ω, denoted by the arrow 44, and the translational motion along the x-axis, denoted by the arrow 46.

As a consequence, a plurality of spiral traces 49 is formed, for example, on an inner surface of a body lumen, as seen in Figure 18D.

Preferably, the motions of the block 90 are contained within the overall structure 20, so that the external surface of the camera 10 remains stationary, wherein the external surface of the camera is substantially transparent to nuclear radiation.

EXAMPLE 3A

Referring further to the drawings, Figures 19A – 19E schematically illustrate the radioactive-emission camera 10, of the single block 90 of a plurality of the detecting units 12.

For understanding the motion of the camera 10 of the present example, it is desirable to define a cylindrical coordinate system of a longitudinal axis, x, and a

radius r, wherein the motion around the longitudinal axis, x, is denoted by ω, while the motion around the radius r is denoted by ϕ.

The single block 90 has a motion with respect to the overall structure 20, which is performed in steps, as follows:

i. the windshield-wiper like oscillatory motion, around the radius r, in the direction of ±ϕ, as denoted by the arrow 50;

ii. the translational motion along the x-axis, by an amount Δx, to a new measuring position, as denoted by the arrow 46;

iii. after traversing the length of the camera, a rotational motion around the x-axis, in the direction of ω, by an amount Δω, as denoted by the arrow 44, in order to perform the same measurements at a new measuring position of ω.

As a consequence, a plurality of broken line traces 59 is formed, as seen in Figure 19E.

Preferably, the motions of the block 90 are contained within the overall structure 20, so that the external surface of the camera 10 remains stationary, wherein the external surface of the camera is substantially transparent to nuclear radiation.

EXAMPLE 4A

Referring further to the drawings, Figures 20A – 20H schematically illustrate the radioactive-emission camera 10, having at least one pair, or a plurality of pairs of blocks 90, adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrows 50. The oscillatory motions may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown in Figures 20B and 20E, by the arrows 54, and as shown in Figures 20C and 21F by the arrows 56. It will be appreciated that the oscillatory motions need not be synchronized in an antipodal manner. Rather, all the blocks 90 may move in synchronized motion, or each block 90 may move independently. It will be appreciated that an odd number of blocks 90 is also possible.

Additionally, a rotational motion of the overall structure 20, around the x-axis in the direction of ω, an amount Δω, to a new measuring position along ω, is provided, after each step of the oscillatory motion, as shown in Figure 20D, by an arrow 52.

The resultant traces are the plurality of broken line traces 59, as seen in Figure 20G.

In essence, the camera 10 of Figures 20A – 20F and 20H provides views which are essentially the same as those of Figures 19A – 19E, but in a more efficient way, since a plurality of blocks is involved.

In accordance with the present example,

i. The different blocks 90 provide views from different orientations; and

ii. The different blocks 90 may change their view orientations.

Preferably, the motions of the blocks 90 are contained within the overall structure 20, so that the external surface of the camera 10 remains stationary, wherein the external surface of the camera is substantially transparent to nuclear radiation.

In particular, as seen in Figure 20H, an internal structure 21 may contain all the blocks 90, configured to move together, as a rigid structure, while the overall structure 20 and the external surface of the camera 10 remain stationary.

The operational manner of the camera 10 of Figures 20A – 20H is described with reference to Figure 23C, hereinbelow.

It will be appreciated that the single detecting units 12 may be used in place of the single blocks 90.

EXAMPLE 5A

Referring further to the drawings, Figures 21A – 21D schematically illustrate the radioactive-emission camera 10, having at least one pair, or a plurality of pairs of blocks 90, adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrow 50. The oscillatory motions are preferably synchronized in an antipodal manner, so as to be diametrically opposed to each other, as in, for example, figure 20B. It will be appreciated that the oscillatory motions need not be synchronized in an antipodal manner. Rather, all the blocks 90 may move in synchronized motion, or each block 90 may move independently. It will be appreciated that an odd number of blocks 90 is also possible.

Additionally, a rotational motion of each of the blocks 90 around the x-axis, in the direction of ω, an amount $\Delta\omega$, to a new measuring position along ω, is provided, after each step of the oscillatory motion, as shown in Figure 21B, by the arrows 44.

This is unlike Figure 20D, wherein the internal structure 21 moved as a rigid unit, as shown in Figure 20D and 20H.

The resultant traces are the plurality of broken line traces 59, as seen in Figure 21D. In essence, the camera 10 of Figures 21A – 21C provides views which are essentially the same as those of Figure 19E, and of Figure 20G, but in a different manner.

In accordance with the present example,

i. The different blocks 90 provide views from different orientations; and

ii. The different blocks 90 may change their view orientations.

Preferably, the motions of the blocks 90 are contained within the overall structure 20, so that the external surface of the camera 10 remains stationary, wherein the external surface of the camera is substantially transparent to nuclear radiation.

It will be appreciated that the detecting units 12 may be used in place of the blocks 90.

EXAMPLE 6A

Referring further to the drawings, Figures 22A – 22C and 22E – 22G schematically illustrate the radioactive-emission camera 95, comprising the plurality of assemblies 92, each assembly 92 being similar in construction to the structure 21 of Figure 20H, in accordance with embodiments of the present invention.

The plurality of assemblies 92 are preferably arranged in parallel, and their rotational motions, around the x-axis, may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown in Figures 22C, by arrows 62, and in Figure 22G, by arrows 64. It will be appreciated that the rotational motion around the x-axis need not be synchronized in an antipodal manner, and may be performed in parallel, or independently.

Thus, the resultant traces are a large plurality of the broken line traces 66 and 68, as seen in Figures 22D and 22H.

In essence, the camera 95 provides views which are essentially the same as those of Figures 19E, 20G, and 21D, but far more efficiently, since a plurality of assemblies is involved.

In accordance with the present example,

i. The different blocks 90 provide views from different orientations;

ii. The different blocks 90 may change their view orientations;

iii. The different assemblies 92 provide views from different orientations; and

iv. The different assemblies 92 may change their view orientations.

The operational manner of the camera 95 is described with reference to Figure 23D, hereinbelow, for the at least two assemblies 92A and 92B.

Preferably, the motions of the blocks 90 and of the assemblies 92 are contained within the overall structure 20, so that the external surface of the camera 95 remains stationary, wherein the external surface of the camera 95 is substantially transparent to nuclear radiation.

It will be appreciated that camera 95 may include a plurality of assemblies 92, which are not parallel to each other. For example, the assemblies 92 may be at right angles to each other, or at some other angle.

It will be appreciated that the assemblies 92 may include the detecting units 12 rather then the blocks 90.

Referring further to the drawings, Figures 22I – 22X schematically illustrate possible individual motions for blocks 90, in accordance with embodiments of the present invention.

In essence, in the present example, the blocks 90 are not arranged in assemblies 92, and each moves independently of the other blocks 90.

In accordance with a first embodiment, of Figures 22I – 22M, each of the blocks 90 may be in communication with two motion providers, for providing the oscillatory motion about the r-axis, as seen by the arrows 50, and for providing the rotational motion around the x-axis, as seen by the arrows 44.

A first set of measurements is performed as the blocks 90 oscillate about the r-axis, as seen in Figure 22J.

The blocks 90 then rotate around the x-axis, to a new measuring position, as seen in Figure 22K.

A second set of measurements is performed at the new position, as the blocks 90 oscillate about the r-axis, as seen in Figure 22M.

The blocks then rotate around the x-axis, to a new measuring position, as shown in Figure 22K, and so on.

The resultant traces are a large plurality of the broken line traces 66 and 68, as seen in Figures 22J and 22M, and are substantially the same as those of Figures 22D and 22H.

In accordance with a second embodiment, each of the blocks 90 (Figure 22N) may be in communication with two motion providers, for providing an oscillatory motion about the x-axis as seen by an arrow 61, and a rotational motion around the x-axis, as seen by an arrows 63. The resultant trace is star shaped, as seen by the lines 65 of Figure 22O.

Additionally, a tertiary motion provider may be included, for providing a cluster 67 of overlapping lines, for a substantially complete coverage of a region, for example, as seen in Figure 22P by a cluster 67 of the overlapping star-shaped lines 65.

It will be appreciated that many other forms of motion may be provided, and may include one, two, three or more motion providers.

Figures 22Q and 22R illustrate another set of dual motions and corresponding measurements for an individual one of the blocks 90, while Figures 22S and 22T illustrate those of a set of a tertiary motion, by three motion providers.

Similarly, Figures 22U and 22V illustrate still another set of two rotational motions and corresponding measurements, provided for each block individually, and Figures 22W and 22X illustrate still another set of a rotational motion, provided for each block individually, and coupled with a linear motion.

It will be appreciated that each block 90, or detecting unit 12 may be provided with at least one, and preferably, two, three, or possibly as many as six degrees of motion, for example, rotational motion around the x, y, and z, axis, or oscillatory motion about these axes, and possibly also translational motion, along the x, and (or) y, and (or) the z-axis. In this manner, each block 90 may be preprogrammed to view each portion of the body section 230, in accordance with some predetermined schedule, dedicated to the specific block 90. For example, one of the blocks 90 may perform oscillatory motion, while an adjacent one of the blocks 90 may perform rotational motion.

Referring further to the drawings, Figures 22Y and 22AA schematically illustrate a center of viewing 200A, for a given camera design, in accordance with embodiments of the present invention.

As the detecting units 12, or blocks 90, or assemblies 92 move or sweep across the region-of-interest volume U, for example, as illustrated by the arrows 203, different portions of the volume U are viewed at different frequencies and duration. The region which is viewed most heavily may be defined as the center of viewing 200A. It is surrounded by regions, which are viewed somewhat less. In essence, a shell-like viewing structure may be formed, with decreasing viewing intensities, as the distance from the center of viewing 200A increases. This is illustrated, for example, by the center of viewing 200A and surrounding shells 201, 209, and 211.

It will be appreciated that the center of viewing 200A may be a region of uniform viewing, rather than a mere point. For example, the region 201 may be a region of uniform viewing, which forms the center of viewing 200A.

EXAMPLE 7A

Having designed a radioactive-emission camera capable of obtaining a collection of views, and having predefined a set of views, which is optimal for a body structure, based on its model, the task of performing measurements, selectively at the predefined set of views, would be quite impossible if it were to be performed manually. Generally, between several hundred and several thousand views are taken, and manually tuning each to a predetermined location, orientation, and possibly also duration would be impractical. Therefore, the camera and method of the present invention are operative with an overall system, in which computer controlled motion providers govern the motions of the detecting units or of the overall camera. The computer may be any one of a personal computer, a laptop, a palmtop, or another computer, adapted for communication with the camera, or a microcomputer, built into the camera. Additionally, a combination of a microcomputer, built into the camera, and an external computer such as a personal computer, a laptop, a palmtop, or the like, may be used.

Preferably, before measurements are performed, personal details are fed into the computer, and the models of the body structure and anatomical constraints are adapted to these details. The personal details may include age, sex, weight, body type, and the like.

Referring further to the drawings, Figures 23A – 23D schematically illustrate a radioactive-emission camera system 400 in accordance with embodiments of the present invention.

As seen in Figure 23A, the camera system 400 includes the camera 10, having a controller 404, in communication with one or several motion providers 76, for sending signals of the locations and orientations of views to the one or several motion providers 76. The one or several motion providers 76, in turn, govern the motions of one or several of the detecting units 12. The one or several of the detecting units 12 collect the measurements at the predefined locations and orientations and communicate the data to the controller 404. Signals of new locations and orientations are then communicated by the controller 404 to the one or several motion providers 76. Each of the motion providers 76 may control the motion of one of the detecting units 12 or of a plurality of the detecting units 12.

Preferably, the controller 404 registers the location and orientation of each of the detecting unit 12 as it moves. Additionally or alternatively, a position-tracking device may be associated with each of the detecting units 12.

Preferably, a position-tracking device 418 is associated with the camera 10 as a whole, for registering its position with respect to, for example, the body structure 215 (Figure 5A).

A power supply 410 powers the camera 10. Alternatively, power may be supplied from the grid.

Preferably, a transceiver or transmitter 402, reports the measurements to an external computer (not shown). Alternatively, a cable (not shown) may be used. Alternatively, the controller 404 includes a microcomputer, or the like, and performs the data analysis.

Additionally, the transceiver 402 may be adapted to receive input data relating to the personal details of the patient, such as the age, sex, weight, body type, and the like, in order to adjust the model of the body structure, hence the locations and orientations of the predefined, optimal set of views, to the particular patient.

Furthermore, the transceiver 402 may be adapted to receive input data from an ultrasound imager, for providing information such as location, size of the body structure and the like, by ultrasound imaging, in order to adjust the model of the body

structure, hence the locations and orientations of the predefined, optimal set of views, to the particular patient.

Preferably, the motion of the one or several motion providers 76 relates to motion of the detecting units 12, with respect to the camera overall structure 20 (Figure 20H), for example, by the motion of detecting units 222A and 222B (Figure 13E), with respect to the overall structure 220, as shown by the arrows 216 and 218.

Alternatively or additionally, the motion of the one or several motion providers 76 may relate to motion of the overall structure 20 or 220 as a whole, for example, as taught with reference to Figure 13E, by the motion the camera 220, as shown by the arrows 224 and 228.

It will be appreciated that the controller 404, while being part of the system 400, need not part of the actual camera 10. Rather it may be an external computer, communicating with the camera 10 either by cables or via a transceiver.

As seen in Figure 23B, the camera 10 includes the blocks 90, each comprising a plurality of the detecting units 12, each block 90 moving as a single body.

As seen in Figure 23C, the individual motion of the blocks 90 is governed by a secondary motion provider 78. Additionally, all of the blocks 90 form an assembly 92, which moves by the motion provider 76, for example, within an internal structure 21, as illustrated hereinbelow with reference to Figure 20H. For example, the secondary motion provider 78 may provide the motion described by the arrows 50 of Figures 20B and 20C or 20F and 20F, hereinbelow while the motion provider 76 may provide the motion described by the arrow 52 of Figure 20H, hereinabove.

It will be appreciated that the multiple motions may be provided to the detecting units 12, rather then to the blocks 90.

It will be appreciated that a tertiary motion provider may also be used and that many arrangements for providing the motions are possible, and known.

As seen in Figure 23D, at least two assemblies 92 may be provided, each with a dedicated motion provider 76 and a dedicated secondary motion provider 78. It will be appreciated that the multiple motions may be provided to the detecting units 12, rather then to the blocks 90. It will be appreciated that tertiary motion providers may also be used and that many arrangements for providing the motions are possible, and known.

In the example of Figure 23D, the controller 404, while being part of the system 400, may not be part of the actual camera 10. For example, it may be an external computer, communicating with the camera 10 either by cables or via a transceiver.

Examples of camera systems for specific applications

Reference is now made to the following examples of radioactive-emission cameras and camera systems, for specific applications.

EXAMPLE 8A

Referring further to the drawings, Figures 24A - 32 schematically illustrate the radioactive-emission camera 10, for the prostate, in accordance with an embodiment of the present invention.

Figures 24A – 24C schematically illustrate the modeling of a prostate and a location of pathology, as a process of two iterations, for zooming in on the pathology, in accordance with embodiments of the present invention.

Figure 24A schematically illustrates a body section 230, which includes a prostate 260, which has sections 262, 264 and 266, and a pathology 265 in section 264. Additionally, the body section 230 includes a rectum 268, from which the prostate 260 may be viewed.

Figure 24B schematically illustrates the model 200 of the body section 230, including the prostate 260, of sections 262, 264 and 266, and the rectum 268. An optimal set of views is predefined based on the model 200 and a first scoring function. The first scoring function may be based on regions of interest similar to the pathology 265, as known, from medical records of common pathologies. Measurements of radioactive emission are then taken at the predefined views, in vivo, for the prostate 260.

As seen in Figure 24C, upon discovering the pathology 265, by the in-vivo measurements, a second model 250 of the section 264 is made, for zooming in on the pathology 265, and a second optimal set of views is predefined, based on the second model 250 of the section 264 and a second scoring function, for zooming in on the pathology 265. Measurements of radioactive emission are then taken at the predefined second set of views, in vivo, for the section 264 and the pathology 265.

It will be appreciated that the first and second scoring functions may be based on any one of or a combination of the information theoretic measures of uniformity, separability, and reliability. It will be further appreciated that the first and second scoring functions need not be the same.

Figures 25A – 25E illustrate an external appearance and an internal structure, of the camera 10. The radioactive-emission camera 10 for the prostate has an extracorporeal portion 80 and an intracorporeal portion 82, which is adapted for insertion into a rectum. The overall structure 20 of the intracorporeal portion 82 is preferably shaped generally as a cylinder and defines a longitudinal axis along the x-axis, and a radius, perpendicular to the longitudinal axis. The intracorporeal portion 82 preferably includes two pairs of assemblies 90, arranged in the overall structure 20. It will be appreciated that another number of assemblies, for example, a single pair, or three pairs, is similarly possible. An odd number of assemblies is similarly possible. In essence, the camera 10 of the present example is analogous to the camera 10 of Figure 23C and Figures 20A - 20F and 20H, and particularly, to Figure 20H. The rotational motion, in the direction of the arrow 52 of Figure 20H, is provided by a motor 88 (Figure 25C) and a main shaft 85. The motor 88 may be an electric motor, for example, a servo motor. The motor 88 and main shaft 85, together, form a motion provider 76 for the rotational motion in the direction of the arrow 52 of Figure 20H. The oscillatory motion, in the direction of the arrows 50 of Figure 20B, is provided by a secondary motor 86, a secondary shaft 84 and a motion transfer link 74. The secondary motor 86 may also be an electric motor, for example, a servo motor. The secondary motor 86, secondary shaft 84 and the motion transfer link 74, together, form the secondary motion provider 78, in the direction of the arrows 224 and 228 of Figures 13E.

The significance of the present embodiment, is as follows:

i. The different assemblies 90 provide views from different orientations; and

ii. The different assemblies 90 may change their view orientations independent of each other.

It is important to point out that during the operation of the camera 10, the external surface of the intracorporeal portion 82 (Figure 25A) remains stationary, while the internal structure 21 (Figure 25C) rotates around the x-axis. The external

surface of the intracorporeal portion 82 may be formed of a carbon fiber, a plastic, or another material, which is substantially transparent to nuclear radiation.

Figure 25E illustrates further the internal structure of the radioactive-emission camera for the prostate, in accordance with an embodiment of the present invention, showing the assemblies 90 within the overall structure 20. Each assembly may be a single detecting unit 12, or a plurality of the detecting units 12, for example, 36 of the detecting units 12, for example, as an array of 6X6, or 99 of the detecting units 12, for example, as an array of 11 X 9, or another number of the detecting units 12, arranged as an array or arranged in another geometry.

Referring further to the drawings, Figure 26 illustrates further the internal structure of the radioactive-emission camera for the prostate, in accordance with an embodiment of the present invention, showing the oscillatory motion (in the direction of the arrows 50 of Figures 20A, and 20C) of the assemblies 90 within the overall structure 20.

Figures 27 – 28 schematically illustrate the radioactive-emission camera 10, for the prostate, in accordance with another embodiment of the present invention. In accordance with the present embodiment, the camera 10 further includes an ultrasound transducer 85, arranged, for example, at the tip of the intracorporeal portion 82.

Figure 27 illustrates the external appearance of the camera 10 with the ultrasound transducer 85 at its tip.

Figure 28 illustrates the ultrasound wave 87, impinging on the prostate 260.

Figures 29A - 29C illustrate the co-registering of a radioactive-emission image and an ultrasound image, to illustrate the functional information of the radioactive-emission image with the structural information of the ultrasound image. The ultrasound image is seen in Figure 29A, the radioactive-emission image is seen in Figure 29B, and the co-registering of the two is seen in Figure 29C.

Figure 30 schematically illustrates the radioactive-emission camera 10, for the prostate, in accordance with another embodiment of the present invention. In accordance with the present embodiment, the camera 10 further includes an ultrasound transducer 85, and a surgical needle 83, in a needle guide 81, arranged alongside the camera 10, for obtaining a biopsy or for other minimally invasive

procedures. Figure 30 schematically illustrates the surgical needle 83 as it penetrates the prostate 260 from the rectum 268.

Figures 31 and 32 schematically illustrate the manner of guiding the needle 83. A track 89 shows the surgeon the direction of the needle, while the camera 10 produces the functional image of the pathology 265 in the prostate 260. By moving the camera 10, manually, the surgeon can align the track 89 with the pathology 265, as shown in Figure 32. Once aligned, he can insert the needle 83, as shown in Figure 30.

EXAMPLE 9A

Referring further to the drawings, Figure 33 pictorially illustrates the method 340 for zooming in on a suspected pathological feature in a woman's reproductive system, as a process of two or more iterations, in accordance with embodiments of the present invention, as follows:

As seen in Figure 33, the method 340 may be described, pictorially, as follows:

In I: The region-of-interest 200, associated with a woman's reproductive system 270, is defined for the body section 230 having the body structure 215.

In II: The model 250 of the volume U, is provided for the region-of-interest 200, possibly with one or several of the modeled organ targets HS, and within the anatomical constraints AC, for obtaining the optimal set of views for the region-of-interest 200. The optimal set of views is then applied to the body section 230.

In III: When a suspected organ target 213 is identified, in vivo, by radioactive-emission measurements at the optimal set of views, a second, inner region-of-interest 200’ is defined, encircling the suspected pathological feature.

In IV: A model 250’ of a volume U’ is provided for the second, inner region-of-interest 200’, preferably, with at least one modeled organ target HS, simulating the suspected organ target 213, for obtaining an optimal pathology set of views for the region-of-interest 200’. The second, pathology set of views is then applied to the body section 230.

Referring further to the drawings, Figures 34A – 34R schematically illustrate radioactive-emission measuring cameras 600, tailored for imaging the woman's reproductive system 270 and optimized with respect to the functional information

gained, regarding the body structures of the woman's reproductive system, such as the cervix 274, the uterus 276, the ovaries 278, and the fallopian tubes 280 (Figure 33), in accordance with preferred embodiments of the present invention.

Figure 34A schematically illustrates the basic radioactive-emission measuring camera 600, for a body lumen, for example, the vagina 272, the cervix 274, the uterus 276, the rectum (not shown), or the sigmoid colon (not shown). The camera 600 includes an extracorporeal portion 610, which preferably comprises a control unit, and an intracorporeal portion 630, having proximal and distal ends 631 and 633, with respect to an operator (not shown).

The control unit of the extracorporeal portion 610 may include control buttons 612 and possibly a display screen 614, and may provide connections with a computer station. It may receive power from a grid or be battery operated. The control unit of the extracorporeal portion 610 may further include a computer or a microcomputer. It will be appreciated that the control unit may be incorporated with the intracorporeal section 630, and operated remotely.

The intracorporeal portion 630 defines a cylindrical coordinate system of x;r, wherein x is the longitudinal axis. The plurality of blocks 90 along the length of the intracorporeal portion 630 is housed in an internal structure 21 (Figure 20H).

Each of the blocks 90 is adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrows 50. The oscillatory motions may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove in Figures 20B and 20E, by the arrows 54, and as shown hereinabove in Figures 20C and 20F by the arrows 56. However, other motions are also possible. For example, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

Additionally, the internal structure 21 is adapted for rotational motion around the x-axis, in the direction of ω, wherein after each step of oscillatory motion at a certain orientation of ω, the internal structure rotates by a step to a new orientation of ω, and the oscillatory motion is repeated.

As a consequence, a plurality of broken line traces 59 are formed, in the body section 230, as seen in Figure 34J.

Preferably, the controller or the computer registers the locations and orientations of each detecting unit or block and correlates the measurements with the corresponding positions and orientations.

A position-tracking device 635 may also be used, for providing information regarding the position of the camera 600 relative to a known reference. For example, if a structural scan, or another scan by another imager has been made, the position-tracking device 635 may be used to register that scan with the measurements of the camera 600.

It will be appreciated that the camera 600 may include detecting units 12 rather then blocks 90.

Preferably, the overall structure 20 remains stationary and is substantially transparent to nuclear radiation, formed, for example, of a hydrocarbon material.

The intracorporeal portion 630 may further include dedicated electronics 634 and motion providers 636, such as miniature motors and motion transfer systems, as known.

Figures 34B and 34C schematically illustrate side and distal views, respectively, of the radioactive-emission measuring camera 600, having an ultrasound imager 640 at its distal tip 633. The ultrasound imager 640 may provide a structural image which may be correlated with the functional image. Additionally, it may be used for providing the size and location of the body structure for modeling. Furthermore, it may be used for providing attenuation correction to the radioactive emission measurements.

Figures 34D and 34E schematically illustrate side and distal views, respectively, of the radioactive-emission measuring camera 600, having an MRI imager 642 at its distal tip 633. The MRI imager 642 may provide a structural image which may be correlated with the functional image. Additionally, it may be used for providing the size and location of the body structure for modeling. Furthermore, it may be used for providing attenuation correction to the radioactive emission measurements.

Figures 34F - 34I schematically illustrate the radioactive-emission measuring camera 600, having a distal block 90A at its distal tip 633. The distal block 90A at the distal tip is also adapted for oscillatory motion, but about the x-axis, as seen by an

arrow 53. When combined with the rotational motion around the x-axis, it produces traces 55 in the shape of a star, in the body section 230, as seen in Figure 34K.

It will be appreciated that a single distal detecting unit may be employed in place of the distal block 90A.

Figures 34L – 34Q schematically illustrates the radioactive-emission measuring camera 600, for a body lumen, having the distal block 90A at its distal tip 633, adapted for a deployed and a retracted position, and for oscillatory motion about the x-axis, when deployed. The camera 600 further has the ultrasound imager 640 at its distal tip 633, as a ring, similarly having a deployed and a retracted position.

Figures 34N – 34P illustrate the distal block 90A deployed, and the ultrasound imager 640 retracted. In this manner, the ultrasound imager 640 does not obstruct the oscillatory motion of the distal block 90A at the distal tip 633.

Figure 34Q illustrates the distal block 90A retracted and the ultrasound imager deployed so the distal block 90A does not obstruct the view of the ultrasound imager. It will be appreciated that the ultrasound image is to be taken once, from the distal tip 633, while the radioactive-emission measurements are to be taken at a plurality of orientations, from the distal tip 633.

Figure 34R illustrates the camera 600 with a cable 620 connecting the intracorporeal portion 630 and the extracorporeal portion 610, for example, for imaging the ovaries and the fallopian tubes from the sigmoid colon.

It will be appreciated that the cameras 600 of the present invention may also be moved manually, both linearly, into the body lumen and rotationally, around its longitudinal axis, preferably while the position-tracking device 635 (Figure 34A) registers its position.

It will be appreciated that a camera with a single block or a single detecting unit may also be used.

EXAMPLE 10A

Referring further to the drawings, Figures 35A – 35Q schematically illustrate radioactive-emission measuring cameras 600, adapted for the esophagus, in accordance with preferred embodiments of the present invention.

Figure 35A schematically illustrates the basic radioactive-emission measuring camera 600, for the esophagus. The camera 600 includes an extracorporeal portion

610, which comprises a control unit, and an intracorporeal portion 630, having proximal and distal ends 631 and 633, with respect to an operator (not shown). A flexible cable 620 connects between them.

The control unit 610 may include control buttons 612 and possibly a display screen 614, and may provide connections with a computer station. It may receive power from a grid or be battery operated. The control unit 610 may further include a computer or a microcomputer.

The intracorporeal portion 630 is constructed essentially as the camera 10 of Figures 23C and Figures 20A – 20H, and specifically, Figure 20H.

Thus, the intracorporeal section 630 defines a cylindrical coordinate system of x;r, wherein x is the longitudinal axis. The plurality of blocks 90 along the intracorporeal portion 630 is housed in an internal structure 21.

Each of the blocks 90 is adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrows 50. The oscillatory motions may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove in Figures 20B and 20E, by the arrows 54, and as shown hereinabove in Figures 20C and 20F by the arrows 56. However, other motions are also possible. For example, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

Additionally, the internal structure 21 is adapted for rotational motion around the x-axis, in the direction of ω, wherein after each step of oscillatory motion at a certain orientation of ω, the internal structure 21 rotates by a step to a new orientation of ω, and the oscillatory motion is repeated.

As a consequence, a plurality of broken line traces 59 are formed, in the body section 230, as seen in Figure 35J.

Preferably, the controller or the computer registers the locations and orientations of each detecting unit or block and correlates the measurements with the corresponding positions and orientations.

A position-tracking device 635 may also be used, for providing information regarding the position of the camera relative to a known reference.

It will be appreciated that the camera 600 may include detecting units 12 rather then blocks 90.

Preferably, the overall structure 20 remains stationary, and has an external surface, which is substantially transparent to nuclear radiation.

A ball bearing 632 may be used at the connecting point with the cable 620, to enable the rotational motion.

The intracorporeal section 630 may further include dedicated electronics 634 and motion providers 636, such as miniature motors and motion transfer systems, as known. Alternatively, the motion may be transferred via the cable 620.

Figures 35B and 35C schematically illustrate side and distal views, respectively, of the radioactive-emission measuring camera 600, for the esophagus, having an ultrasound imager 640 at its distal tip 633. The ultrasound imager 640 may provide a structural image which may be correlated with the functional image. Additionally, it may be used for providing the size and location of the relevant organ for modeling. Furthermore, it may be used for providing attenuation correction to the radioactive emission measurements.

Figures 35D and 35E schematically illustrate side and distal views, respectively, of the radioactive-emission measuring camera 600, for the esophagus, having an MRI imager 642 at its distal tip 633. The MRI imager 642 may provide a structural image which may be correlated with the functional image. Additionally, it may be used for providing the size and location of the relevant organ for modeling. Furthermore, it may be used for providing attenuation correction to the radioactive emission measurements.

Figures 35F - 35I schematically illustrate the radioactive-emission measuring camera 600, for the esophagus, having a block 90 at its distal tip 633. The block 90 at the distal tip is also adapted for oscillatory motion, but about the x-axis, as seen by an arrow 53. When combined with the rotational motion around the x-axis, it produces traces 55 in the shape of a star, in the body section 230, as seen in Figure 35K.

Figures 35L – 35Q schematically illustrates the radioactive-emission measuring camera 600, for the esophagus, having a block 90 at its distal tip 633, adapted for a deployed and a retracted position, and for oscillatory motion about the x-axis, when deployed. The camera 600 further has the ultrasound imager 640 at its distal tip 633, as a ring, similarly having a deployed and a retracted position.

Figures 35N – 35P illustrate the block 90 deployed, and the ultrasound imager 640 retracted. In this manner, the ultrasound imager 640 does not obstruct the oscillatory motion of the block 90 at the distal tip 633.

Figure 35Q illustrates the block 90 retracted and the ultrasound imager deployed so the block 90 does not obstruct the view of the ultrasound imager. It will be appreciated that the ultrasound image is to be taken once, from the distal tip 633, while the radioactive-emission measurements are to be taken at a plurality of orientations, from the distal tip 633.

Figures 36A and 36B schematically illustrates the body section 230, showing an esophagus 650. The radioactive-emission measuring camera 600 for the esophagus (Figures 35A – 35Q), is adapted for oral insertion, through a mouth 652, and is further designed for identifying pathological features in a neck area 654, for example, as relating to the vocal cords, the thyroid gland, the submandibular glands. Additionally, it is designed for identifying pathological features in the trachea 656, the lungs 658, the heart 660, the breasts, the stomach 662, the pancreas 664, and the liver 666, as well as other relevant organs and glands, for example, the lymph glands.

The camera system of the present invention allows imaging of internal organs from a close proximity. Additionally, it is particularly advantageous for overweight people and for women with large breasts, for whom extracorporeal imaging, for example, extracorporeal cardiac imaging by nuclear emission measurements, is ineffective, because of losses in the tissue.

For cardiac imaging, the radiopharmaceuticals associated with the camera of Figures 35A – 35Q may be Myoview™(technetium Tc-99m tetrofosmin), a cardiac imaging agent, of GE Healthcare, GE Medical Systems, http://www.gehealthcare.com/contact/contact_details.html#diothers. Alternatively, it may be Cardiolite (Sestamibi radilabeled with Tc-99m), of DuPont, http://www1.dupont.com/NASApp/dupontglobal/corp/index.jsp?page=/content/US/en_US/contactus.html. It will be appreciated that other agents may be used, as known, for other relevant organs, for example, for the detection of cancerous tissue or other pathologies.

In accordance with the preferred embodiment of the present invention, cardiac imaging is performed with Teboroxime, for example, for myocardial perfusion imaging.

It will be appreciated that the radioactive-emission measuring camera 600, for the esophagus of the present invention may also be used in parallel with the cardiac camera system 500 of Example 12, described hereinbelow.

EXAMPLE 11A

Referring further to the drawings, Figures 37- 39 schematically illustrate the body section 230, as a heart, which includes the region-of-interest 200, associated with the organ 215, being the heart, which includes an aorta 242, a left atrium 244 and a right atrium 246.

Figure 38 schematically illustrates a second, inner region-of-interest 200', associated with the aorta 242.

Similarly, Figure 39 schematically illustrates a second, inner region-of-interest 200', associated with the left atrium 244.

Referring further to the drawings, Figures 40 – 52E schematically illustrate a cardiac camera system 500, in accordance with a preferred embodiment of the present invention.

Figures 40 – 45 schematically illustrate the basic components of the cardiac camera system 500, in accordance with embodiments of the present invention. These include an operator computer station 510, a chair 520, and a radioactive-emission camera assembly 530.

As seen in Figure 43, computer station 510 may be further adapted for input of an ultrasound imager 535, for example, a handheld ultrasound imager 535, possibly with a position-tracking device 537, or a 3-D ultrasound imager. The data provided by the ultrasound imager 535 may be used in the modeling of the heart. Preferably, the data of the ultrasound imager may be co-registered with the radioactive emission measurements, on the same frame of reference, for providing co-registration of structural and functional images. It will be appreciated that the imager 535 may be an MRI imager.

A problem in cylindrical volumes, when viewed along the periphery of the cylinder is that the innermost information is blocked by the concentric information around it. Thus, it is often advisable to obtain views from the bases of the cylinder.

Figure 44 schematically illustrate a camera 530A, which includes shoulder sections 530B, for viewing the heart essentially from a base of the cylindrical volume, in accordance with embodiments of the present invention.

Figure 45 schematically illustrate cameras 530B, formed as shoulder sections for viewing the heart essentially from a base of the cylindrical volume, in accordance with an alternative embodiment of the present invention.

Views from the shoulders, either as in Figure 44 or 45 provides information not blocked or hidden by the chest.

It will be appreciated that the design of cameras 530B is possible because of the small size of the blocks 90 relative to the contour or of the body section 230.

Figure 46 schematically illustrates the chair 520 and the camera assembly 530, arranged for operation, in accordance with a preferred embodiment of the present invention. Preferably, the chair 520 is in a partial reclining position, and the camera assembly 530 is designed to face it, opposite the chest of a person sitting on the chair 520. Preferably, the camera assembly 530 includes a housing, operative as the overall structure, which is substantially transparent to radioactive emission. Alternatively, a skeleton, which is open on the side facing a patient, may be usedd as the overall structure.

It will be appreciated that another chair or a bed may be used rather than the chair 520. Alternatively, the patient may be standing.

Figures 47 – 48 schematically illustrate possible inner structures of the camera assembly, in accordance with preferred embodiments of the present invention.

Figure 47 schematically illustrates the inner structure of the camera assembly 530, showing the overall structure 20, the parallel lines of assemblies 92, possibly of an even number, each with a dedicated motion provider 76 and a dedicated secondary motion provider 78, and the rows of blocks 90, possibly arranged in pairs, along the assemblies 92.

The camera assembly 530 defines an internal frame of reference 80, while each assembly 92 has a reference cylindrical coordinate system of x;r, with rotation around x denoted by ω and rotation around r denoted by ϕ, wherein the oscillatory motion about r is denoted by the arrow 50.

Preferably, the motion of the camera assembly 530 corresponds to that described hereinabove, with reference to Figures 20A – 20H and 22A – 22H, as follows:

The plurality of blocks 90 is adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrow 50. The oscillatory motions may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove in Figures 20B and 20E, by the arrows 54, and as shown hereinabove in Figures 20C and 20F by the arrows 56. However, other motions are also possible. For example, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

Furthermore, the plurality of assemblies 92 are preferably arranged in parallel, and their rotational motions, around the x-axis, in the direction of ω, may also be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove, in Figures 22C, by arrows 62, and as shown hereinabove in Figure 22G, by arrows 64. However, other motions are also possible. For example, the assemblies 92 may move together, or independently. It will be appreciated that an odd number of assemblies 92 is also possible.

Thus, the resultant traces are a large plurality of the broken line traces 59, as seen hereinabove, with reference to Figures 22D and 22H, on the chest of the patient.

In accordance with the present example,

i. The different blocks 90 provide views from different orientations;

ii. The different blocks 90 may change their view orientations;

iii. The different assemblies 92 provide views from different orientations; and

iv. The different assemblies 92 may change their view orientations.

The operational manner of the camera 530 is described hereinbelow with reference to Figure 23D, for the at least two assemblies 92.

Preferably, the motions of the blocks 90 and of the assemblies 92 are contained within the overall structure 20, so that the external surface of the camera assembly 530 remains stationary, wherein the external surface of the camera assembly 530 is substantially transparent to nuclear radiation. Alternatively, the overall structure may be a skeleton, open on the side facing the patient.

It will be appreciated that the oscillatory motions need not be synchronized in an antipodal manner. Rather, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

It will be appreciated that camera 530 may include a plurality of assemblies 92, which are not parallel to each other. For example, the assemblies 92 may be at right angles to each other, or at some other angle. It will be appreciated that the assemblies 92 may include detecting units 12 rather then blocks 90, for example, as in the camera 10 of Figures 20A – 20G.

Figure 48 schematically illustrates a section 531 of the camera assembly 530, showing the inner structure thereof, in accordance with another embodiment of the present invention. Accordingly, the camera assembly 530 may include the overall structure 20, and a single one of the assemblies 92, within the overall structure 20, having the dedicated motion provider 76, the dedicated secondary motion provider 78, and the rows of blocks 90. Additionally, in accordance with the present embodiment, the camera assembly 530 includes a tertiary motion provider 77, for sliding the assembly 90 laterally, in the directions of the arrow 75, along the chest of the patient (not shown). In this manner, imaging of the chest may be performed with the single assembly 92.

Figures 49A and 49B schematically illustrate the assembly 92 and the block 90, in accordance with a preferred embodiment of the present invention. In essence, the assembly 92 is constructed in a manner similar to the camera 10 of Figures 20A – 20H, and specifically Figure 20H, and according to Figure 23D, hereinabove.

Thus the assembly 92 includes a row of at least two blocks 90, each adapted for oscillatory motion about r. The blocks 90 are arranged within the internal structure 21.

A motor 88 and a shaft 85 form the motion provider 76, while a secondary motor 86 and a secondary shaft 84 form the secondary motion provider 78, for the oscillatory motion about r. A plurality of motion transfer systems 74, for example gear systems, equal in number to the number of blocks 90, transfer the motion of the secondary motion provider 78 to the blocks 90. The motion transfer systems 74, for example, of gears, make it possible to provide the row of blocks 90 with any one of parallel oscillatory motion, antipodal oscillatory motion, or independent motion,

depending on the gear systems associated with each block 90. It will be appreciated that other motion transfer systems, as known, may be used.

It will be appreciated that detecting units 12 may be used in place of blocks 90.

In accordance with the present example, adjacent blocks 90A and 90B may move in an antipodal manner and adjacent blocks 90C and 90D may move in an antipodal manner, while adjacent blocks 90B and 90C may move in parallel. It will be appreciated that many other arrangements are similarly possible. For example, all the pairing combinations of the blocks 90 may move in an antipodal manner, all the blocks 90 may move in parallel, or the blocks 90 may move independently. It will be appreciated that an odd number of blocks 90 may be used in the assembly 92.

Figure 50 schematically illustrates the block 90, in accordance with a preferred embodiment of the present invention. The block 90 includes a frame 93, which houses the detector material 91, which is preferably pixelated, and the collimators 96. Additionally, the frame 93 houses dedicated electronics 97, preferably on a PCB board 99. Furthermore, where several modules of the detector material 91 need to be used, a structural element 89 may be provided to hold the different modules of the detector material 91 together. It will be appreciated that a single pixel detector may be used. Alternatively, a single module of a pixelated detector may be used. Alternatively, the block 90 may be constructed as any of the examples taught with reference to Figures 17A – 17N, or as another block, as known.

The dimensions, which are provided in Figure 50, are in mm. It will be appreciated that other dimensions, which may be larger or smaller, may similarly be used.

FIGURE 51 schematically illustrates the cardiac model 250, in accordance with a preferred embodiment of the present invention. The cardiac model 250 includes the volume U, for example, as a cylinder, and the anatomical constraints AC. The rows of blocks 90 are arranged around the volume U, as permissible by the anatomical constraints AC.

FIGURES 52A – 52E schematically illustrate the blocks 90, arranged for viewing the cardiac model 250, in accordance with a preferred embodiment of the present invention.

In Figure 52A, the block 90 is shown with the frame 93, which houses the detector material 91, which is preferably pixelated, and the collimators 96. Additionally, the frame 93 houses the dedicated electronics 97, on the PCB board 99.

In Figure 52B, fields of view 98 of the blocks 90 are seen for a situation wherein adjacent blocks 90A and 90B move in an antipodal manner, while adjacent blocks 90B and 90C move in a nearly parallel manner. The figure illustrates that when moving in an antipodal manner, the blocks 90 do not obstruct each other's field of view 98. Yet, when moving in a parallel manner, or a near parallel manner, obstruction may occur.

A similar observation is made by Figure 52C, wherein the adjacent blocks 90B and 90C move in an antipodal manner, while the adjacent blocks 90A and 90B move in a near parallel manner.

Again, it will be appreciated that many other arrangements are similarly possible. For example, all the pairing combinations of the blocks 90 may move in an antipodal manner, all the blocks 90 may move in parallel, or the blocks 90 may move independently. It will be appreciated that an odd number of blocks 90 may be used in the assembly 92.

Figure 52D illustrates possible dimensions for the cardiac model 250. The dimensions are in mm. It will be appreciated that other dimensions are similarly possible. Furthermore, it will be appreciated that the model 250 may be based on general medical information of the organ 215 and common pathological features associated with it. Additionally, the model may be based on information related to a specific patient, such as age, sex, weight, and body type. Furthermore, a structural image, such as by ultrasound or MRI, may be used for providing information about the size and location of the heart 215 in relation to the body section 230 (Figure 5A), for generating the model 250.

Figure 52E schematically illustrates a possible arrangement of the blocks 90 for viewing the volume U of the model 250, within the anatomical constrains AC. The significance of the present invention, as illustrated by Figures and 52E is that all the blocks maintain a close proximity to the modeled volume U, and to the region-of-interest, in vivo, even as they move. This is in sharp contrast to the prior art, for example, as taught by US Patent 6,597,940, to Bishop, et al, and US Patent 6,671,541, to Bishop, in which the blocks are fixed within a rigid overall structure, so that as

some of the blocks are placed in close proximity to the body, others are forced away from the body, and their counting efficiency deteriorates.

Preferably, the radiopharmaceuticals associated with the camera of Figures 40 – 52E may be Myoview™(technetium Tc-99m tetrofosmin), a cardiac imaging agent, of GE Healthcare, GE Medical Systems, http://www.gehealthcare.com/contact/contact_details.html#diothers. Alternatively, it may be Cardiolite (Sestamibi radilabeled with Tc-99m), of DuPont, http://www1.dupont.com/NASApp/dupontglobal/corp/index.jsp?page=/content/US/en_US/contactus.html. It will be appreciated that other agents may be used.

In accordance with the preferred embodiment of the present invention, esophagus imaging is performed with Teboroxime as the radiopharmaceutical.

It will be appreciated that cardiac imaging, in accordance with embodiments of the present invention relates to the imaging of the whole heart, or to a portion of the heart, or to blood vessels near the heart, for example, the coronary artery.

EXAMPLE 12A

Referring further to the drawings, Figure 53 schematically illustrates a dual imaging system 700 for radioactive-emissions in tandem with a three-dimensional structural imager, in accordance with a preferred embodiment of the present invention.

The dual imaging system 700 includes a three-dimensional structural imager 720, preferably, on a structural-imager gantry 722, and a radioactive-emission measuring camera 730, preferably, on a camera gantry 732. A patient 750 may lie on a bed 740, which is adapted for motion into the radioactive-emission measuring camera 730 and the three-dimensional structural imager 720, on a bed gantry 742.

A control unit 710 controls the operation of the dual system 700, including the three-dimensional structural imager 720, the radioactive-emission measuring camera 730, and the bed 740. The control unit 710 may also analyze the data.

Alternatively, two control units may be used, one for controlling the three-dimensional structural imager 720 and another for controlling the radioactive-emission measuring camera 730. It will be appreciated that the control system of the radioactive-emission measuring camera 730 generally controls the order of the

operation of the dual system 700, wherein the radioactive-emission measuring may be performed before or after the structural imaging.

It will be further appreciated that the radioactive-emission measuring camera 730 may be configured as an add-on system, adapted for operating with an existing structural imager. It may be supplied with a dedicated software, for example, in a CD format, or with its own control unit, which is preferably adapted for communication with the structural imager control unit.

The three-dimensional structural imager 720 may be, for example, a CT or an MRI, which defines a frame of reference, wherein the radioactive-emission measuring camera 730 is co-registered to the frame of reference.

In this manner, co-registration of functional and structural images is possible. Additionally, the structural image may be used for providing tissue information for attenuation correction of the functional image, resulting in a more accurate functional image.

The radioactive-emission measuring camera 730 may be constructed as one arc 730A, preferably adapted for viewing a full width of a body from a single position of the camera 730. Alternatively, the radioactive-emission measuring camera 730 may be constructed as two arcs 730A and 730B, which are adapted for viewing a full circumference of a body, from a single position of the camera 730. It will be appreciated that the camera 730 may have other geometries, for example, a circle, an ellipse, a polygon, a plurality of arcs forming a circle, or a plurality of sections, forming a polygon, or other shapes.

Preferably, where the camera 730 is adapted for viewing a full circumference of a patient, from a single position, the bed 740 is formed as a stretcher, with a sheet 744, which is substantially transparent to radioactive emission, for example, of a hydrocarbon material.

Figure 54 schematically illustrates a cross-sectional view of dual imaging system 700 for radioactive-emissions in tandem with a three-dimensional structural imager, in accordance with a preferred embodiment of the present invention.

Preferably, the gantry 732 of the camera 730 is adapted for vertical motion, as described by the arrows 734, so as to bring the camera 730 closer to the patient 750.

Additionally, the gantry 722 of the three-dimensional structural imager 720 may be adapted for rotation, as described by an arrow 724.

The bed 740 is preferably adapted for motion into and out of the camera 730 and the three-dimensional structural imager 720.

Preferably, the rate of imaging by the three-dimensional structural imager 720 and by the radioactive-emission measuring camera is substantially the same, so the bed moves into the two imagers at a constant speed.

In accordance with embodiments of the present invention, the camera 730, formed of portions 730A and 730B, as illustrated in Figures 53 and 54 may also be a radioactive-emission measuring PET camera. Additionally, while the patient 750 appears lying, the patient may be sitting standing, lying on the back or lying on the stomach.

It will be appreciated that the body structure that may be imaged may be an organ, such as a heart or a pancreas, a gland, such as a thyroid gland or a lymph gland, blood vessels, for example, the coronary artery or the pulmonary artery, a portion of an organ, such as an aorta or a left atrium of a heart, a bone, a ligament, a joint, a section of the body, such as a chest or an abdomen, or a whole body.

Preferably, the radiopharmaceuticals associated with the camera of the present invention be any one of the following:

1. anti-CEA, a monoclonal antibody fragment, which targets CEA – produced and shed by colorectal carcinoma cells – and may be labeled by Tc-99m or by other radioisotopes, for example, iodine isotopes (Jessup JM, 1998, Tumor markers – prognostic and therapeutic implications for colorectal carcinoma, Surgical Oncology; 7: 139-151);

2. In-111-Satumomab Pendetide (Oncoscint®), designed to target TAG-72, a mucin-like glycoprotein, expressed in human colorectal, gastric, ovarian, breast and lung cancers, but rarely in healthy human adult tissues [Molinolo A; Simpson JF; et al., 1990, Enhanced tumor binding using immunohistochemical analyses by second generation anti-tumor-associated glycoprotein 72 monoclonal antibodies versus monoclonal antibody B72.3 in human tissue, Cancer Res., 50(4): 1291-8];

3. Lipid-Associated Sialic Acid (LASA), a tumor antigen, used for colorectal carcinoma, with a similar sensitivity as anti-CEA monoclonal antibody fragment but a greater specificity for differentiating between benign and malignant lesions (Ebril KM, Jones JD, Klee GG, 1985, Use and limitations of serum total and

lipid-bound sialic acid concentrations as markers for colorectal cancer, Cancer; 55:404-409);

4. Matrix Metaloproteinase-7 (MMP-7), a proteins enzyme, believed to be involved in tumor invasion and metastasis (Mori M, Barnard GF et al., 1995, Overexpression of matrix metalloproteinase-7 mRNA in human colon carcinoma, Cancer; 75: 1516-1519);

5. Ga-67 citrate, used for detection of chronic inflammation (Mettler FA, and Guiberteau MJ, Eds., 1998, Inflammation and infection imaging, Essentials of nuclear medicine, Fourth edition, Pgs: 387-403);

6. Nonspecific-polyclonal immunoglobulin G (IgG), which may be labeled with both In-111 or Tc-99m, and which has a potential to localize nonbacterial infections (Mettler FA, and Guiberteau MJ, ibid);

7. Radio-labeled leukocytes, such as such as In-111 oxine leukocytes and Tc-99m HMPAO leukocytes, which are attracted to sites of inflammation, where they are activated by local chemotactic factors and pass through the endothelium into the soft tissue [Mettler FA, and Guiberteau MJ, ibid; Corstens FH; van der Meer JW, 1999, Nuclear medicine's role in infection and inflammation, Lancet; 354 (9180): 765-70]; and

8. Tc-99m bound to Sodium Pertechnetate, which is picked up by red blood cells, and may be used for identifying blood vessels and vital organs, such as the liver and the kidneys, in order to guide a surgical instrument without their penetration.

Additionally, certain organic materials can replace normal atoms in organic molecules with radioactive atoms, and thus can be used to label metabolism. In general, these are used for PET imaging. However, they can be used for other nuclear imaging as well. The radionuclides may be, for example:

1. F-18 fluoro-deoxyglucose (FDG)

2. F-18 Sodium Fluoride

3. C-11 methionine

4. Other less common C-11 amino acid tracers, such as:

C-11 thymidine,

C-11 tyrosine,

C-11 leucine

5. N-13 ammonia
6. O-15 water
7. Rb-82 Rubidium Rb-82
8. Cu-62 copper
9. Ga-68 gallium

In accordance with the preferred embodiment of the present invention, the dual imaging and any whole body imaging may be performed with Teboroxime as the radiopharmaceutical.

It will be appreciated that other agents may be used.

Figures 55A – 55C schematically illustrate possible inner structures of the camera 730, in accordance with preferred embodiments of the present invention.

Figure 55A schematically illustrates the inner structure of the camera 730, showing the overall structure 20 and the parallel lines of the assemblies 92, possibly of an even number, each with the row of blocks 90, possibly arranged in pairs. Each of the assemblies 92 preferably includes the dedicated motion provider 76, for providing the rotational motion around x, and the dedicated secondary motion provider 78, for providing the oscillatory motion about r in the direction of the arrow 50.

The camera 730 defines an internal frame of reference 80, while each assembly 92 has a reference cylindrical coordinate system of x;r, with rotation around x denoted by ω and rotation around r denoted by ϕ, wherein the oscillatory motion about r is denoted by the arrow 50.

Preferably, the motions of the assemblies 92 and the blocks 90 correspond to those described hereinabove, with reference to Figures 20A – 20H and 22A – 22H, as follows:

The plurality of blocks 90 is adapted for the windshield-wiper like oscillatory motion, around the radius r, as denoted by the arrow 50. The oscillatory motions may be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove in Figures 20B and 20E, by the arrows 54, and as shown hereinabove in Figures 20C and 20F by the arrows 56. However, other motions are also possible. For example, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

Furthermore, the plurality of assemblies 92 are preferably arranged in parallel, and their rotational motions, around the x-axis, in the direction of ω, may also be synchronized in an antipodal manner, so as to be diametrically opposed to each other, as shown hereinabove, in Figures 22C, by arrows 62, and as shown hereinabove in Figure 22G, by arrows 64. However, other motions are also possible. For example, the assemblies 92 may move together, or independently. It will be appreciated that an odd number of assemblies 92 is also possible.

Thus, the resultant traces are a large plurality of the broken line traces 59, as seen hereinabove, with reference to Figures 22D and 22H, on the skin of the patient.

In accordance with the present example,

i. The different blocks 90 provide views from different orientations;

ii. The different blocks 90 change their view orientations;

iii. The different assemblies 92 provide views from different orientations; and

iv. The different assemblies 92 change their view orientations.

The operational manner of the camera 730 is described hereinbelow with reference to Figure 23D, for the at least two assemblies 92.

Preferably, the motions of the blocks 90 and of the assemblies 92 are contained within the overall structure 20, so that the overall structure 20 of the camera 730 remains stationary, wherein the external surface of the camera 730 is substantially transparent to nuclear radiation. Alternatively, the overall structure may be a skeleton, open on the side facing the patient.

It will be appreciated that the oscillatory motions need not be synchronized in an antipodal manner. Rather, the blocks 90 may move together, or independently. It will be appreciated that an odd number of blocks 90 is also possible.

It will be appreciated that the camera 730 may include a plurality of assemblies 92, which are not parallel to each other. For example, the assemblies 92 may be at right angles to each other, or at some other angle. It will be appreciated that the assemblies 92 may include detecting units 12 rather then blocks 90, for example, as in the camera 10 of Figures 20A – 20G.

Figure 55B schematically illustrates a section 731 of the camera 730, showing the inner structure thereof, in accordance with another embodiment of the present invention. Accordingly, the camera 730 may include the overall structure 20, and a

single one of the assemblies 92, within the overall structure 20, having the dedicated motion provider 76, the dedicated secondary motion provider 78, and the rows of blocks 90. Additionally, in accordance with the present embodiment, the camera 730 includes a tertiary motion provider 77, for sliding the assembly 90 laterally, in the directions of an arrow 75.

Figure 55C schematically illustrates an alternative arrangement of the blocks 90 around the volume U of the model 250, wherein each of the blocks 90 is provided with motion around the x-axis, in the direction of ω, and with the oscillatory motion about r, preferably in the y-z plane, as illustrated by the arrow 50. Accordingly, the assemblies 92 need not be used. Rather, each of the blocks 90 may communicate with two motion providers which provide it with the two types of motion.

Figures 56A and 56B schematically illustrate the assembly 92 and the block 90, in accordance with a preferred embodiment of the present invention. In essence, the assembly 92 is constructed in a manner similar to the camera 10 of Figure 20H, and according to Figure 23D, hereinabove.

Thus the assembly 92 includes a row of at least two blocks 90, each adapted for oscillatory motion about r. The blocks 90 are arranged within the internal structure 21.

A motor 88 and a shaft 85 form the motion provider 76, while a secondary motor 86 and a secondary shaft 84 form the secondary motion provider 78, for the oscillatory motion about r. A plurality of motion transfer systems 74, for example gear systems, equal in number to the number of blocks 90, transfer the motion of the secondary motion provider 78 to the blocks 90. The motion transfer systems 74, of gears, make it possible to provide the row of blocks 90 with any one of parallel oscillatory motion, antipodal oscillatory motion, or independent motion, depending on the gear systems associated with each block 90. It will be appreciated that other motion transfer systems, as known, may be used.

It will be appreciated that detecting units 12 may be used in place of blocks 90.

In accordance with the present example, adjacent blocks 90A and 90B may move in an antipodal manner and adjacent blocks 90C and 90D may move in an antipodal manner, while adjacent blocks 90B and 90C may move in parallel. It will be appreciated that many other arrangements are similarly possible. For example, all the pairing combinations of the blocks 90 may move in an antipodal manner, all the

blocks 90 may move in parallel, or the blocks 90 may move independently. It will be appreciated that an odd number of blocks 90 may be used in the assembly 92.

It will be appreciated that many other cameras and camera systems may be considered and the examples here are provided merely to illustrate the many types of combinations that may be examined, in choosing and scoring a camera design, both in terms of information and in terms of secondary considerations, such as rate of data collection, cost, and complexity of the design.

EXAMPLE 13A

Brain cancer is the leading cause of cancer-related death in patients younger than age 35, and in the United States, the annual incidence of brain cancer generally is 15–20 cases per 100,000 people.

There are two types of brain tumors: primary brain tumors that originate in the brain and metastatic (secondary) brain tumors that originate from cancer cells that have migrated from other parts of the body.

Approximately 17,000 people in the United States are diagnosed with primary cancer each year; nearly 13,000 die of the disease. Amongst children, the annual incidence of primary brain cancer is about 3 per 100,000.

Primary Brain Tumors are generally named according to the type of cells or the part of the brain in which they begin. The most common are gliomas, which begin in glial cells, and of which there are several types, as follows:

Astrocytoma, a tumor which arises from star-shaped glial cells called astrocytes, which most often arises in the cerebrum in adults, whereas, in children, it occurs in the brain stem, the cerebrum, and the cerebellum;

Brain stem glioma, a tumor that occurs in the lowest part of the brain and is diagnosed in young children as well as in middle-aged adults;

Ependymoma, a tumor most common in middle-aged adults, which arises from cells that line the ventricles or the central canal of the spinal cord, and also occurs in children and young adults; and

Oligodendroglioma, a rare tumor, which arises from cells that make the fatty substance that covers and protects nerves and usually occurs in the cerebrum, grows slowly and generally does not spread into surrounding brain tissue.

Some types of brain tumors do not begin in glial cells. The most common of these are:

Medulloblastoma, also called a primitive neuroectodermal tumor, a tumor which usually arises in the cerebellum and is the most common brain tumor in children;

Meningioma, which arises in the meninges and usually grows slowly;

Schwannoma, also called an acoustic neuroma, and occurring most often in adults, it is a tumor that arises from a Schwann cell, of the cells that line the nerve that controls balance and hearing, in the inner ear;

Craniopharyngioma, a tumor which grows at the base of the brain, near the pituitary gland, and most often occurs in children;

Germ cell tumor of the brain, a tumor which arises from a germ cell, generally, in people younger than 30, the most common type of which is a germinoma; and

Pineal region tumor, a rare brain tumor, which arises in or near the pineal gland, located between the cerebrum and the cerebellum.

Certain inherited diseases are associated with brain tumors, for example, Multiple endocrine neoplasia type 1 (pituitary adenoma), Neurofibromatosis type 2 (brain and spinal cord tumors), Retinoblastoma (malignant retinal glioma), Tuberous sclerosis (primary brain tumors), and Von Hippel-Lindau disease (retinal tumor, CNS tumors). Furthermore, genetic mutations and deletions of tumor suppressor genes (i.e., genes that suppress the development of malignant cells) increase the risk for some types of brain cancer.

Additionally, exposure to vinyl chloride is an environmental risk factor for brain cancer. Vinyl chloride is a carcinogen, used in the manufacturing of plastic products such as pipes, wire coatings, furniture, car parts, and house wares, and is present in tobacco smoke. Manufacturing and chemical plants may release vinyl chloride into the air or water, and it may leak into the environment as a result of improper disposal. People who work in these plants or live in close proximity to them have an increased risk for brain cancer.

Secondary brain cancer occurs in 20–30% of patients with metastatic disease and its incidence increases with age. In the United States, about 100,000 cases of secondary brain cancer are diagnosed each year. Patients with a history of melanoma, lung, breast, colon, or kidney cancer are at risk for secondary brain cancer.

Brain tumors can obstruct the flow of cerebrospinal fluid (CSF), which results in the accumulation of CSF (hydrocephalus) and increased intracranial pressure (IICP). Nausea, vomiting, and headaches are common symptoms. They can damage vital neurological pathways and invade and compress brain tissue. Symptoms usually develop over time and their characteristics depend on the location and size of the tumor.

The first step in diagnosing brain cancer involves evaluating symptoms and taking a medical history. If there is any indication that there may be a brain tumor, various tests are done to confirm the diagnosis, including a complete neurological examination, imaging tests, and biopsy.

Referring now to the drawings, Figures 57A – 57F present the principles of modeling, for obtaining an optimal set of views, for a body organ 215, in accordance with embodiments of the present invention.

Figure 57A schematically illustrates a body section 230, illustrating the organ 215, being the brain 215. The brain 215 is enclosed within a skull 830 and includes:

a cerebellum 802, the part of the brain below the back of the cerebrum, which regulates balance, posture, movement, and muscle coordination;

a corpus callosum 804, which is a large bundle of nerve fibers that connect the left and right cerebral hemispheres;

a frontal lobe of the cerebrum 806, which is the top, front regions of each of the cerebral hemispheres, and is used for reasoning, emotions, judgment, and voluntary movement;

a medulla oblongata 808, which is the lowest section of the brainstem (at the top end of the spinal cord) and controls automatic functions including heartbeat, breathing, and the like;

a occipital lobe of the cerebrum 810, which is the region at the back of each cerebral hemisphere, at the back of the head, and contains the centers of vision and reading ability;

a parietal lobe of the cerebrum 812, which is the middle lobe of each cerebral hemisphere between the frontal and occipital lobes, located at the upper rear of the head, and which contains important sensory centers;

a pituitary gland 814, which is a gland attached to the base of the brain that secretes hormones, and is located between the pons and the corpus callosum;